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L1 HAS NO ANSWERS

L1 STR

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40567 TO 46153

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L2 3 SEA SSS SAM L1

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FULL SEARCH INITIATED 13:51:12 FILE 'REGISTRY'
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104 ANSWERS

3 ANSWERS

SEARCH TIME: 00.00.02

L3 104 SEA SSS FUL L1

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=> s 13

L4 55 L3

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- L4 ANSWER 45 OF 55 CAPLUS COPYRIGHT 2006 ACS on STN
- AN 1989:71643 CAPLUS
- DN 110:71643
- TI Substrate specificity of adenosine deaminase: role of methyl groups at 2',3'- and 5'-positions of adenosine
- AU Kalinichenko, E. N.; Beigel'man, L. N.; Mikhailov, S. N.; Mikhailopulo, I.
- CS Inst. Bioorg. Chem., Minsk, USSR
- SO Bioorganicheskaya Khimiya (1988), 14(9), 1157-61 CODEN: BIKHD7; ISSN: 0132-3423
- DT Journal
- LA Russian
- AB The substrate specificity of adenosine deaminase was studied using C'-Me derivs. of adenosine. On the basis of the correlation revealed between conformations of 2'- and 3'-C-methyladenosine and their substrate properties, a modified stereochem. model is suggested: the enzyme accepts the substrate within a N-type conformational range (4E04T303E) of the furanose ring. The model was analyzed in detail using a number of C3'-modified adenosines and 5'-C-methyladenosine analogs with D-allo- and L-talo-configuration.
- IT 15397-12-3

RL: RCT (Reactant); RACT (Reactant or reagent) (reaction of, with adenosine deaminase, kinetics of)

RN 15397-12-3 CAPLUS

Absolute stereochemistry.

L4 ANSWER 46 OF 55 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1988:204993 CAPLUS

DN 108:204993

TI New syntheses of 2'-C-methyl nucleosides starting from D-glucose and D-ribose

AU Beigelman, L. N.; Ermolinskii, B. S.; Gurskaya, G. V.; Tsapkina, E. N.; Karpeiskii, M. Ya.; Mikhailov, S. N.

CS Inst. Mol. Biol., Moscow, USSR

SO Carbohydrate Research (1987), 166(2), 219-32 CODEN: CRBRAT; ISSN: 0008-6215

DT Journal

LA English

OS CASREACT 108:204993

GΙ

AB Effective general methods have been developed for the synthesis of 2'-C-methylnucleosides from D-glucose and D-ribose. 3-O-Benzyl-1,2-O-isopropylidene-3-C-methyl-O-D-allofuranose was prepared in 5 steps from D-glucose and converted into 1,2,3-dtri-O-acetyl-2-C-methyl-5-O-p-methylbenzoyl-D-ribofuranose (I). I was also synthesized from 2-C-hydroxymethyl-2,3-O-isopropylidene-5-O-trityl-D-ribofuranose, prepared in 3 steps from D-ribose. Condensation of I with the bis(trimethylsilyl) derivs. of uracil, N4-benzoylcytosine, and N6-benzoyladenine in the presence of F3CSO3SiMe3 followed by removal of the protecting acyl groups yielded the 2'-C-methylnucleosides.

IT 15397-12-3P

RN 15397-12-3 CAPLUS

CN Adenosine, 2'-C-methyl- (8CI, 9CI) (CA INDEX NAME)

L4 ANSWER 47 OF 55 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1988:146857 CAPLUS

DN 108:146857

TI 2'-, 3'- And 5'-C-Methyl derivatives of uridine in the reaction of microbiological transglycosylation

AU Zinchenko, A. I.; Barai, V. N.; Eroshevskaya, L. A.; Beigel'man, L. N.; Mikhailov, S. N.; Karpeiskii, M. Ya.; Mikhailopulo, I. A.

CS Inst. Mikrobiol., Moscow, USSR

SO Doklady Akademii Nauk SSSR (1987), 297(3), 731-4 [Biochem.] CODEN: DANKAS; ISSN: 0002-3264

DT Journal

LA Russian

AB Transglycosylation of uridine and its Me derivs. was carried out by cell suspensions of Escherichia coli. The reaction was catalyzed by uridine phosphorylase and purine nucleoside phosphorylase which were detected in cell-free exts. The products (adenine nucleosides) from uridine, uracil alloside, and uracil taloside were obtained at a yield of 100, 42, and .2%, resp. 2'-C-Methyluridine and 3-C-methyluridine did not undergo any transglycosylation, suggesting that the 5'-C-Me group is crucial for the reaction to take place.

IT 15397-12-3P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of, by microbial transglycosylation of methyluridine)

RN 15397-12-3 CAPLUS

CN Adenosine, 2'-C-methyl- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 48 OF 55 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1980:560970 CAPLUS

DN 93:160970

TI Adenosine receptor activation in human fibroblasts: nucleoside agonists and antagonists

AU Bruns, Robert F.

CS Dep. Neurosci., Univ. California, La Jolla, CA, 92093, USA

SO Canadian Journal of Physiology and Pharmacology (1980), 58(6), 673-91 CODEN: CJPPA3; ISSN: 0008-4212

DT Journal

LA English

AΒ Adenosine [58-61-7] (ED50 15 μ M) causes a 50-fold increase in intracellular cyclic AMP in the VA13 human fibroblast line. A total of 128 nucleosides was tested as agonists and antagonists. Eight classes of compds. were found: full agonists (14 compds.), weak agonists (20), high-efficacy partial agonists (16), low-efficacy partial agonists (7), competitive inhibitors (11), noncompetitive inhibitors (3), partial agonist - noncompetitive inhibitors (3), and inactive compds. (54). noncompetitive inhibitors antagonized the responses to adenosine, isoproterenol, and prostaglandin E1 and thus may have been adenylate cyclase inhibitors. The most potent noncompetitive inhibitor, 2',5'-dideoxyadenosine [6698-26-6] was a partial inhibitor, reducing the response to isoproterenol by only 77% even at very high concns. The most potent agonists, partial agonists, and pure antagonists had apparent affinities of about 5 μM. Although all positions were important for affinity at the adenosine receptor, only the 3'- and 5'-positions and to a much lesser extent the 6- and 8-positions had an effect on efficacy. The receptor tolerated bulky groups at the 6-position of adenosine, had an Et-sized pocket near the 5'-position, and had little bulk tolerance towards modifications at other positions. Among the full agonists, only one 5'-derivative and one 2-position derivative had higher apparent affinity

than

adenosine. Studies with conformationally restricted agonists and antagonists showed that adenosine must be in the anti conformation in order to bind to the receptor.

IT 15397-12-3

RL: BIOL (Biological study)

(adenosine receptor response to, structure in relation to)

RN 15397-12-3 CAPLUS

CN Adenosine, 2'-C-methyl- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 49 OF 55 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1973:30124 CAPLUS

DN 78:30124

TI Solvolysis of adenine nucleosides. I. Effects of sugars and adenine substituents on acid solvolyses

AU Garrett, Edward R.; Mehta, P. J.

CS Coll. Pharm., Univ. Florida, Gainesville, FL, USA

SO Journal of the American Chemical Society (1972), 94(24), 8532-41 CODEN: JACSAT; ISSN: 0002-7863

DT Journal

LA English

AΒ The acidic solvolyses of 2',3'-dideoxyadenosine > 2'-deoxyadenosine > $9-\beta-D$ -psicofuranosyladenine » 3'-deoxyadenosine > 8-bromoadenosine > 9- β -D-arabinofuranosyladenine .apprx. 2-chloroadenosine .apprx. N6-methyladenosine .gtorsim. adenosine .apprx. 2-methyladenosine > 1-methyladenosine .apprx. N6,N6-dimethyladenosine .gtorsim. $9-\beta-D-xylofuranosyladenine > 8-methoxyadenosine .apprx.$ 2'-C-methyladenosine gave the resp. sugar and stable adenine moiety except in the case of where the resultant 1-methyladenine was more slowly transformed into 5-aminoimidazole-4-N'-methylcarboxamidine. The ranking of relative activities are given above for 80° in 0.10M HCl. Only specific acid catalyzed solvolyses of the protonated and non-protonated species were observed and there was no maximum in solvolysis rate in the low pH region, supporting the argument against a Schiff base intermediate subsequent to ethereal oxygen attack. The probability of an A-1 mechanism for solvolyses of diprotonated adenine nucleosides with protons on the nitrogens in the 1 and 7 positions was favored by the fact that the entropies of activation, $\Delta S.++.$, were close to zero. Although the inductive effect of the 2'-OH inhibited acid solvolysis, a less significant increase in reactivity was introduced by the substitution of a hydrogen for the 3'-OH. The effects of substituents on the pyrimidine ring lead to only minor effects in reactivity whereas substitution of Br or MeO on C-8 of the imidazole portion has a more pronounced effect. The 1-methyladenosine cation solvolyzes in acid at about the same rate as the adenosine cation strongly suggesting that it is the 1-protonated form of the latter that reacts with a second proton to result in a solvolyzing dication.

Absolute stereochemistry.

L4 ANSWER 50 OF 55 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1971:23087 CAPLUS

DN 74:23087

TI Nucleosides of branched-chain nitromethyl, cyanomethyl, and aminomethyl sugars

AU Rosenthal, Alex; Sprinzl, Matej; Baker, Donald A.

CS Dep. Chem., Univ. British Columbia, Vancouver, BC, Can.

SO Tetrahedron Letters (1970), (48), 4233-5 CODEN: TELEAY; ISSN: 0040-4039

DT Journal

LA English

GI For diagram(s), see printed CA Issue.

AB The oxidation of $9-(3,5-0-isopropylidene-\beta-D-xylofuranosyl)$ adenine with

RuO4 gave the 2'-oxo-derivative, which, upon treatment with MeNO2 and NaOMe gave I. Reduction of I with Pd gave 9-(2-C-acetamidomethyl-3,5-O-isopropylidene- β -D-lyxofuranosyl)adenine. The condensation of 1,2:5,6-di-O-isopropylidene- α -D-ribo-hexofuranos-3-ulose with di-Et cyanomethylphosphonate in the presence of NaH, followed by hydrogenation over Pd, gave II. Selective hydrolysis of II followed by benzoylation, hydrolysis of the 1,2-O-isopropylidene group and acetylation gave III. Frsion of III with 6-chloropurine gave 6-chloro-9-(2-O-acetyl-5,6-di-O-benzoyl-3,C-cyanomethyl-3-deoxy- β -D-allofuranosyl)purine which upon treatment with Me2NH gave 6-dimethylamino-9-(3-C-cyanomethyl-3-deoxy- β -D-allofuranosyl)purine.

IT 30737-89-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

RN · 30737-89-4 CAPLUS

CN Adenine, 9-[2-C-(nitromethyl)- β -D-lyxofuranosyl]- (8CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 51 OF 55 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1970:404136 CAPLUS

DN 73:4136

TI Mass spectrometry of nucleic acid components. Analogs of adenosine

AU Shaw, Stanley James; Desiderio, Dominic M.; Tsuboyama, Kaoru; McCloskey, James A.

CS Inst. for Lipid Res., Baylor Coll. of Med., Houston, TX, USA

SO Journal of the American Chemical Society (1970), 92(8), 2510-22 CODEN: JACSAT; ISSN: 0002-7863

DT Journal

LA English

AB The mass spectra of adenosine and 32 of its analogs were studied in detail. Principal fragmentation pathways for structurally significant ions were determined and decomposition mechanisms postulated, based on metastable

transitions, deuterium and substituent labels, and high-resolution mass spectra. The major ions M -30, base +44, and base +30 are proposed to arise from initial transfer of sugar hydroxyl hydrogens to the charge-localized purine base. Methylation at N6 is characterized by elimination of MeN6 with rearrangement of either H or a Me group as previously reported for the corresponding bases. 2'-O-Methylation leads to a unique sugar fragment resulting from elimination of the base plus a 3'- or 5'-hydroxyl H. Anomers are readily distinguished by their mass spectra, but steric orientation of sugar hydroxyls cannot be determined directly. However the abundance of the M - 30 ion was found to depend strongly on the steric accessibility of C-5' to the base.

IT 15397-12-3

RL: PRP (Properties)

(mass spectrum of)
RN 15397-12-3 CAPLUS
CN Adenosine, 2'-C-methyl- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

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ANSWER 52 OF 55 CAPLUS COPYRIGHT 2006 ACS on STN
L4
     1969:502192 CAPLUS
AN
DN
     71:102192
     Substituted purine nucleosides
ΤI
     Walton, Edward
IN
PA
     Merck and Co., Inc.
SO
     Fr., 11 pp.
     CODEN: FRXXAK
DT
     Patent
```

LA French FAN.CNT 1

IAN.C	PATENT NO.		KIND	DATE	APPLICATION NO.	DATE
PI	FR 1521076			19680412	FR 1967-104388	19670427
	DE 1593110				DE	
	DE 1620053				DE	
	DE 1695411				DE	
	DE 1768470				DE	
	DE 1770700				DE	
	GB 1163102	,			GB	
	GB 1187824				GB	
	GB 1187825				GB	
	US 3480613			19691125	US	19670703
PRAI	US			19660502		

The title compds. (I), which were useful in preparing nucleotides for the study of nucleic acid metabolism were prepared by treating 2,6-substituted chloromercuri-purines with 2,3,5,-tri-O-acyl-2-methyl-D-ribofuranosyl halides to give 2,6-substituted 9-(2,3,5,-tri-O-acyl-2-C-methyl-Dribofuranosyl) purines which were solvolyzed, aminolyzed, or mercaptolyzed. Thus, a solution of 5 g. 2-C-methyl-D-ribono-1,4-lactone in 100 cc. dry pyridine at 5° was treated with 17 cc.BzCl, heated 65-70° 4 hrs., and kept at room temperature 6 hrs. to give 60% 2,3,5-tri-O-benzoyl-2-C-methyl-D-ribono-1,4-lactone (II) m. 138-40°. A solution 7 g. II in 30 cc. dry tetrahydrofuran under N was cooled and treated with 58.8 cc. M di-sec-isoamyl-borane, kept at room temperature 16 hrs., 6 cc. H2O added, refluxed 0.5 hr., and at 5°, 11.5 cc. H2O2 added keeping the pH 7-8 by the addition of about 7 cc. 3N Na2CO3 to give 37% 2,3,5-tri-O-benzoyl-2-C-methyl-(α and β)-Dribofuranose (III) purified by chromatog. on silica gel. A solution 4.2 g. III (containing a small amount of 3,5-di-O-benzoyl-2-C-methyl- (α,β) -Dribofuranose) in 80 cc. dry pyridine was treated with 8.0 cc. BzCl and heated at 90° for 4 hrs. to give 42% 1,2,3,5-tetra-O-benzoyl-2-C-

methyl-β-D-ribofuranose (IV), m. 155-6°, and 57%
1,2,3,5-tetra-O-benzoyl-2-C-methyl-α-D-ribofuranose (V) as an oil.
to 100 cc. of a saturated HCl Et2O solution was added 2 cc. AcCl and 1.5 g. IV
and the mixture kept at room temperature 2 hrs. to give
2,3,5-tri-O-benzoyl-2-Cmethyl-β-D-ribofuranosyl chloride (VI) A solution of 1.5 g. V in 7.5

methyl- β -D-ribofuranosyl chloride (VI). A solution of 1.5 g. V in 7.5 cc. AcOH was treated with a solution of 0.25 cc. AcBr and 7.5 cc. 32% HBr in AcOH and the mixture kept at 25° 24 hrs. to give 2,3,5-tri-O-benzoyl-2-C-methyl- β -D-ribofuranosyl bromide. From a suspension of 5.95 g. 2-acetamido-9-chloromercuri-6-hydroxypurine in 175 cc. xylene about 25 cc. of xylene was distilled to remove traces of H2O, the VI prepared from 8.1 g. IV in 25 cc. dry xylene was added, and the mixture stirred at $50-100^{\circ}$ and refluxed 1 hr. to give 2-acetamido-9-(2,3,5-tri-O-benzoyl-2-methyl-Dribofuranosyl)-6-hydroxypurine (VII). Similarly prepared were: 6-N-methyl-9-(2,3,5-tri-O-benzoyl-C-methyl-D-ribofuranosyl)benzamidopurine (VIII); 6-chloro-9-(2,3,5-tri-O-benzoyl-2-C-methyl-D-ribofuranosyl)purine (IX); 2.6-dibenzamido-9-(2.3.5-tri-O-benzoyl-2-C-methyl-Dribofuranosyl)purine (X); 6-methyl-9-(2,3,5-tri-0-benzoyl-2-C-methyl-Dribofuranosyl)purine (XI); 6-benzamido-9-(2,3,5-tri-O-benzoyl-2-C-methyl-Dribofuranosyl)purine (XII). A suspension of 1.0 g. IX in 25 cc. MeOH containing 6.5 g. Me2NH was heated 10 hrs. in a sealed tube at 100° and concentrated in vacuo and the residue dissolved in 25 cc. H2O, washed with C6H6,

and treated with 2 g. Dowex II-X8 strongly basic anion-exchange resin to give I (R1 = Me2N, R = H). A mixture of 1.2 g. X in 12 cc. dry MeOH was treated with 97 mg. Na in 12 cc. MeOH and refluxed 3 hrs. to give I (R =R1 = NH2). A suspension of 1.25 g. IX and 307 mg. thiourea in 3 cc. EtOH was refluxed 40 min. to give 9-(2,3,5-tri-O-benzoyl-2-C-methyl-Dribofuranosyl)purine-6-thiol, (XIII). A suspension of 400 mg. XIII in 3.5 cc. MeOH was treated with a solution prepared from 19.5 mg. Na in 3.5 cc. dry MeOH and the mixture refluxed 3 hrs. to give I (R = H, R1 = SH). A mixture 1 g. IX, 8 g. MeNH2, and 25 g. MeOH was heated at 100° 10 hrs. in a sealed tube to give I(R = H, R1 = NHMe). A solution of 1 g. IX in 17 cc. dioxane, 80 mg. MgO, and 0.5 g. of 5% Pd on C was shaken 98 hrs. in a H atmospheric at 25° to give 9-(2,3,5-tri-O-benzoyl-2-C-methyl-D-ribofuranosyl)purine (XIV). A solution 400 mg. XIV in 8 cc. dry MeOH was treated with a solution of 23 mg. Na in 8 cc. dry MeOH and refluxed 3 hrs. to give I(R = R1 = H). A suspension of 800 mg. VII in 8 cc. anhydrous MeOH was treated with a solution of 105 mg. Na in 8 cc. dry MeOH and the mixture refluxed 2 hrs. to give 9-(2-C-methyl-D-ribofuranosyl)guanine. A solution of 479 mg. IX in 20 cc. MeOH containing 2 g. NH3 was kept at 5° 20 hrs. to give I(R = H, R1 = C1). A suspension of 3.9 g. VIII in 40 cc. dry MeOH was treated with a solution prepared from 175 mg. Na in 40 cc. dry MeOH, and the mixture refluxed 3.5 hrs. to give I(R = H, R1 = MeNH). A solution of 2.0 g. IX in 30 cc. EtOH containing 12 cc. EtNH2 was heated in a sealed tube at 100° for 10 hrs. to give I(R = H, R1 = NHEt). A solution of 605 mg. IX in 30 cc. dry MeOH was treated with a solution prepared by saturating 20

0.1N NaOMe solution with MeSH, and the mixture refluxed 30 min. to give I(R = H, R1 = SMe). A mixture of 590 mg. XI and 50 cc. dry MeOH was treated with a solution prepared from 23 mg. Na and 10 cc. dry MeOH, and the mixture refluxed

4 hrs. to give I(R = H, R1 = Me). A mixture 1.48 g. XII and 15 cc. MeOH was treated with a solution prepared from 70 mg. Na and 5 cc. MeOH, and the mixture refluxed 45 min. to give 59% 2'-C-methyladenosine.

IT 15397-12-3P 25899-60-9P 25899-63-2P 25899-67-6P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

RN 15397-12-3 CAPLUS

CN Adenosine, 2'-C-methyl- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 25899-60-9 CAPLUS

Adenine, N,N-dimethyl-9-(2-C-methyl-D-ribofuranosyl)- (8CI) (CA INDEX CN NAME)

25899-63-2 CAPLUS RN

Adenine, N-methyl-9-(2-C-methyl-D-ribofuranosyl)- (8CI) (CA INDEX NAME) CN

OH

RN 25899-67-6 CAPLUS

Adenine, N-ethyl-9-(2-C-methyl-D-ribofuranosyl)- (8CI) (CA INDEX NAME) CN

L4 ANSWER 53 OF 55 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1969:403610 CAPLUS

DN 71:3610

TI Circular dichroism of nucleoside derivatives. VI. Optically active bands of adenine nucleoside derivatives

AU Miles, Daniel W.; Robins, Morris J.; Robins, Roland K.; Eyring, Henry

CS Univ. of Utah, Salt Lake City, UT, USA

SO Proceedings of the National Academy of Sciences of the United States of America (1969), 62(1), 22-9 CODEN: PNASA6; ISSN: 0027-8424

DT Journal

LA English

AB Structures and circular dichroism (CD) curves with several characteristic absorption curves of 17 purine nucleoside derivs. are presented. The CD data show that the 260 and 207 m μ absorption systems of the adenine chromophore contain at least 2 electronic transitions. The CD maxima, at 260, 240, 220, and 200 m μ , seem related in the 5 major base constituents of nucleic acids and derivs. The optically active transitions at these wavelengths are discussed. Solvent studies other than H2O at pH 7, including EtOH and methylcyclohexane, suggest the CD bands arise from π - π * transitions. A weak absorption band, with little rotatory power, that obeys the criteria of an n- π * band is resolved near 290 m μ in hydrocarbon solvents.

IT 15397-12-3

RL: PRP (Properties)

(circular dichroism of)

RN 15397-12-3 CAPLUS

CN Adenosine, 2'-C-methyl- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 54 OF 55 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1968:436399 CAPLUS

DN 69:36399

TI Branched-chain sugar nucleoside. IV. 2'-Methyladenosine

AU Jenkins, Susan R.; Arison, Byron; Walton, Edward

CS Merck Sharp and Dohme Res. Lab., Rahway, NJ, USA

SO Journal of Organic Chemistry (1968), 33(6), 2490-4 CODEN: JOCEAH; ISSN: 0022-3263

DT Journal

LA English

GI For diagram(s), see printed CA Issue.

The synthesis of 2'-C-methyladenosine (I) is described. The required AB derivative of the previously unknown 2-C-methyl-D-ribofuranose was prepared starting with 2-C-methyl-D-ribono-1,4-lactone (II). II was completely benzoylated and the Bz derivative reduced with bis-(3-methyl-2-butyl)borane which produced a mixture of 2,3,5-tri-O-benzoyl-2-C-methyl- α (and β)-D-ribofuranose and 3,5-di-O-benzoyl-2-C-methyl- α (and β)-D-ribofuranose. This mixture was benzoylated to give a mixture of α and β tetrabenzoates which was converted into 2,3,5-tri-O-benzoyl-2-C-methyl- β -D-ribofuranosyl chloride (III). reacted with chloromercuri-6-benzamidopurine to give the completely acylated nucleoside. Catalytic removal of the Bz blocking groups with NaOMe in MeOH led to the isolation of cryst.I. From N.M.R. spectral measurements and consideration of steric interactions, it is suggested that I exists in a 2'-oxo-3'-endo (T23) conformation and is, therefore, conformationally unrelated to adenosine. 18 references.

IT 15397-12-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

RN 15397-12-3 CAPLUS

CN Adenosine, 2'-C-methyl- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 55 OF 55 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1967:95342 CAPLUS

DN 66:95342

TI Branched-chain sugar nucleosides. New type of biological active nucleoside

AU Walton, Edward; Jenkins, Susan R.; Nutt, Ruth F.; Zimmerman, Morris; Holly, Frederick W.

CS Merck Sharp und Dohme Res. Labs., Rahway, NJ, USA

SO Journal of the American Chemical Society (1966), 88(19), 4524-5 CODEN: JACSAT; ISSN: 0002-7863

DT Journal

LA English

AB 2'-C-Methyladenosine (I) and 3'-C-methyladenosine (II), the first nucleosides of branched-chain sugars, were prepared in a search for analogs resistant to adenosine deaminase (LaPage and Junga, CA 62, 4429c). I was deaminated at a rate only 1/25th that of adenosine and II was not affected. At a concentration of 10 μg./ml. they had 65 to 80% inhibitory

effect on KB cells in culture (Gitterman, et al., CA 63, 10496h). I was synthesized from 2,3,5-tri-O-benzoyl- α -D-glucosaccharinic acid lactone through reduction with bis(3-methyl-2-butyl)borane to 2,3,5-tri-O-benzoyl-2-C-methyl- α (and β)-D-ribofuranose and benzoylation to the tetrabenzoate which was resolved by chromatography into a solid (III) (presumably β) and a sirup (IV) (presumably α). III and IV were converted into the same chloro derivative (V) by ethereal HCl, conversion of III being more rapid, probably because of an anchimeric effect. V reacted with chloromercuri-6-benzamidopurine to give amorphous 9-(2,3,5-tri-O-benzoyl-2-C-methyl- β -D-ribofuranosyl)-6-benzamidopurine, which was purified on silica gel and was converted by NaOMe into I.

IT 15397-12-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

RN 15397-12-3 CAPLUS

CN Adenosine, 2'-C-methyl- (8CI, 9CI) (CA INDEX NAME)

14530,627

=> s 200362256/pn

L9 0 200362256/PN

=> s wo 200362256/pn

L10 1 WO 200362256/PN

(WO2003062256/PN)

=> sel rn

E1 THROUGH E39 ASSIGNED

=> file req

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FULL ESTIMATED COST

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(1068-57-1/RN)

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(107-15-3/RN)

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(109-84-2/RN)

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(1117-97-1/RN)

1 141-43-5/BI

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(205171-05-7/RN)

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(22195-47-7/RN)

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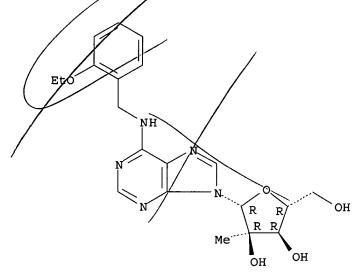
L11

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=> d scan 111

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN IN Adenosine, N-[(2-ethoxyphenyl)methyl]-2'-C-methyl- (9CI) MF C20 H25 N5 O5

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):38

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN

IN Hydrazine, methyl- (6CI, 8CI, 9CI)

MF C H6 N2

CI COM

 $H_3C-NH-NH_2$

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Adenosine, N-[(2,2-dimethyl-1,3-dioxolan-4-yl)methyl]-2'-C-methyl- (9CI)
MF C17 H25 N5 O6

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN

IN 1,2-Ethanediamine (9CI)

MF C2 H8 N2

CI COM

 $H_2N-CH_2-CH_2-NH_2$

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN IN Adenosine, N-(2-hydroxyethyl)-2'-C-methyl- (9CI) MF C13 H19 N5 O5

Absolute stereochemistry.

HO

NH

N

R

R

R

OH

OH

OH

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN IN Ethanol, 2-hydrazino- (6CI, 7CI, 8CI, 9CI)

MF C2 H8 N2 O CI COM

HO-CH2-CH2-NH-NH2

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN IN Adenosine, N,N-bis(2-hydroxyethyl)-2'-C-methyl- (9CI) MF C15 H23 N5 O6

Absolute stereochemistry.

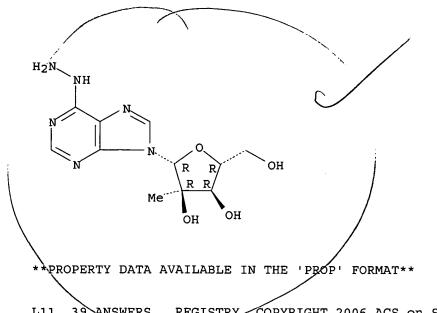
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN IN Ethanol, 2-amino- (8CI, 9CI)

MF C2 H7 N O
CI COM

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN IN Inosine, 2'-C-methyl-, hydrazone (9CI) MF C11 H16 N6 O4



L1139 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN

IN Benzeneethanamine, β -methyl- (9CI)

MF C9 H13 N

CI COM

$$\begin{array}{c} \text{Ph} \\ | \\ \text{Me-CH-CH}_2 - \text{NH}_2 \end{array}$$

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN Inosine, 2'-C-methyl-, 2,2-dimethylhydrazone (9CI) MF C13 H20 N6 O4

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 39 ANSWERS RÉGISTRY COPYRIGHT 2006 ACS on STN

IN Hydrazinecarboxaldehyde (9CI)

MF C H4 N2 O

CI COM

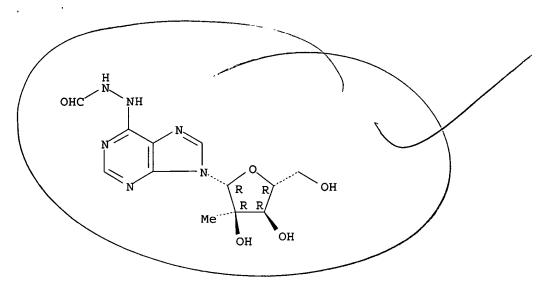
 $O = CH - NH - NH_2$

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Ethanol, 2-[1-[9-(2-C-methyl-β-D-ribofuranosyl)-9H-purin-6yl]hydrazino]- (9CI)
MF C13 H20 N6 O5

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN IN Acetic acid/ hydrazide (6CI, 7CI, 8CI, 9CI) MF C2 H6 N2 O CI COM $H_2N-NH-C$ CH₃ **PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT** L11/39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN IN Inosine, 2'-C-methyl-, formylhydrazone (9CI) C12 H16 N6 O5 MF



L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN

IN Methanamine, N-methoxy- (9CI)

MF C2 H7 N O

CI COM

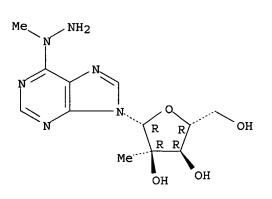
H₃C-NH-O-CH₃

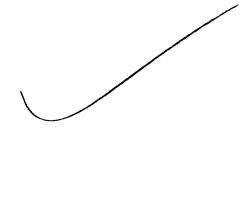
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN

MF C12 H18 N6 O4

Absolute stereochemistry.





PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN

IN Benzenamine, 3-(methylthio)- (9CI)

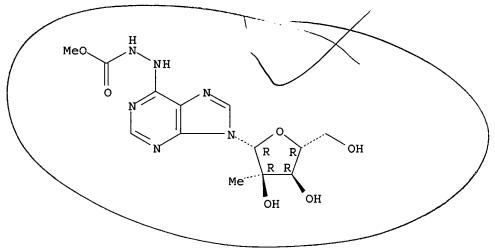
MF C7 H9 N S

CI COM

Absolute stereochemistry.

C13 H18 N6 O6

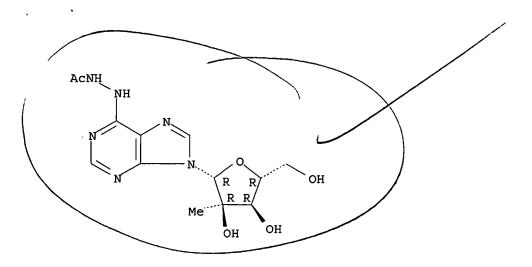
MF



purin-6-yl]-, methyl ester (9CI)

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

```
L11
    39 ANSWERS
                  REGISTRY COPYRIGHT 2006 ACS on STN
IN
     Hydrazinecarboxylic acid, methyl ester (9CI)
MF
     C2 H6 N2 Q2
CI
     COM
MeO-O-NH-NH2
  PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**
L11
    39 ANSWERS
                  REGISTRY COPYRIGHT 2006 ACS on STN
IN
     Acetic acid, 2-[9-(2-C-methyl-β-D-ribofuranosyl)-9H-purin-6-
     yl]hydrazide (9CI)
MF
     C13 H18 N6 O5
```

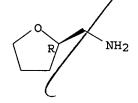


L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN IN 2-Furanmethanamine, tetrahydro-, (2R)- (9CI)

MF C5 H11 N O

CI COM

Absolute stereochemistry. Rotation (-).



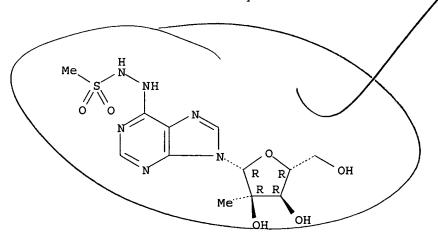
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN

IN Methanesulfonic acid, 2-[9-(2-C-methyl-β-D-ribofuranosyl)-9H-purin-6yl]hydrazide (9CI)

MF C12 H18 N6 O6 S

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN IN Inosine, 2'-C-methyl-, oxime (9CI) MF C11 H15 N5 O5

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Carbamic acid, hydroxy-, 1,1-dimethylethyl ester (9CI)
MF C5 H11 N O3
CI COM

t-BuO-C-NH-OH

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN

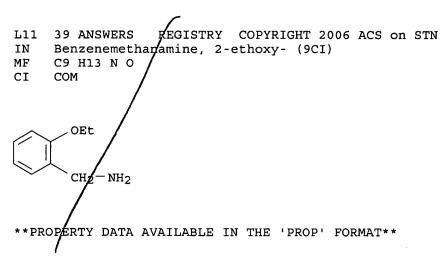
Adenosine, N-methoxy-N-methyl-2'-C-methyl- (9CI)

Absolute stereochemistry.

C13 H19 N5 O5

IN

MF

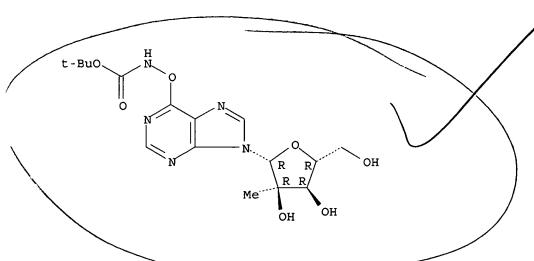


L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN

IN Carbamic acid, [[9-(2-C-methyl-β-D-ribofuranosyl)-9H-purin-6-yl]oxy], 1,1-dimethylethyl ester (9CI)

MF C16 H23 N5 07

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROD' FORMAT

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN

IN 9H-Purine, 6-chloro-9-(2,3,5-tri-O-benzoyl-2-C-methyl-β-Dribofuranosyl)- (9CI)
MF C32 H25 Cl N4 O7

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN IN Carbamic acid, [[9-(2-C-methyl- β -D-ribofuranosyl)-9H-purin-6-yl]oxy]-, phenylmethyl ester (9CI) MF C19 H21 N5 O7

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN IN 9H-Purine, 6-chloro-9-(2-C-methyl- β -D-ribofuranosyl)- (9CI) MF C11 H13 Cl N4 O4

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN IN Adenosine, N-(2-aminoethyl)-2'-C-methyl- (9CI) MF C13 H20 N6 O4

Absolute stereochemistry.

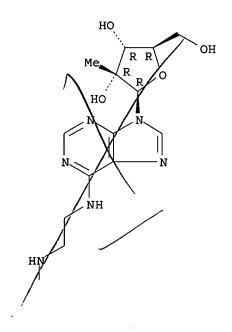
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN IN Adenosine, 2'-C-methyl-N-[3-(methylthio)phenyl]- (9CI) MF C18 H21 N5 O4 S

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN IN Adenosine, N,N''-1,2-ethanediylbis[2'-C-methyl- (9CI) MF C24 H32 N10 O8

Absolute stereochemistry.

PAGE 1-A



L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN IN Adenosine, 2'-C-methyl-N-(2-phenylpropyl)- (9CI) MF C20 H25 N5 O4

Absolute stereochemistry.

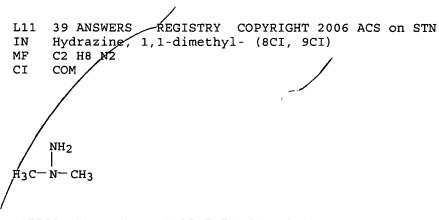
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN IN Inosine, 2'-C-methyl-, O-methyloxime (9CI) MF C12 H17 N5 O5

L11 39 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Adenosine, 2'-C-methyl-N-[[(2R)-tetrahydro-2-furanyl]methyl]- (9CI)
MF C16 H23 N5 O5

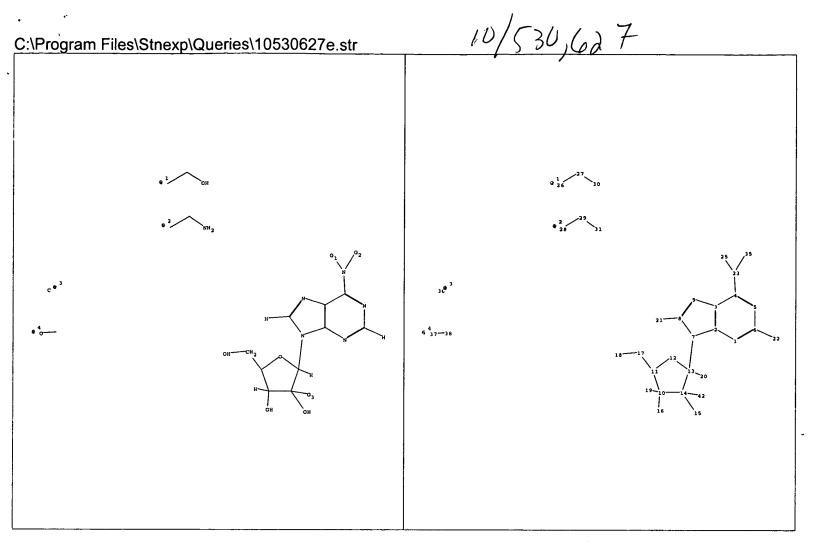
Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED



chain nodes:

15 16 17 18 19 20 21 22 23 25 26 27 28 29 30 31 35 37 42

ring nodes:

1 2 3 4 5 6 7 8 9 10 11 12 13 14

ring/chain nodes:

36 38

chain bonds:

4-23 6-22 7-13 8-21 10-16 10-19 11-17 13-20 14-15 14-42 17-18 23-25 23-35 26-27 27-30 28-29 29-31 37-38

ring bonds:

1-2 1-6 2-3 2-7 3-4 3-9 4-5 5-6 7-8 8-9 10-11 10-14 11-12 12-13 13-14

exact/norm bonds:

2-7 3-9 4-23 7-8 7-13 8-9 10-11 10-14 10-16 11-12 12-13 13-14 14-15 14-42 23-25 23-35 27-30 29-31 37-38

exact bonds:

6-22 8-21 10-19 11-17 13-20 17-18 26-27 28-29

normalized bonds:

1-2 1-6 2-3 3-4 4-5 5-6

G1:CH3,NH2,H

G2:CH3,OH,MeO,[*1],[*2]

G3:CN,[*3],[*4]

Search for independent claims 2+3 where Z is G3 + X II

- N < G,

Match level:

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:CLAS\$16:CLAS\$17:CLAS\$18:CLAS\$19:CLAS\$20:CLAS\$21:CLAS\$22:CLAS\$23:CLAS\$25:CLAS\$25:CLAS\$26:CLAS\$28:CLAS\$29:CLAS\$30:CLAS\$31:CLAS\$35:CLAS\$36:CLAS\$37:CLAS\$38:CLAS\$36:CLAS

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LOGINID:ssspta1600txm

PASSWORD:

* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * * * SESSION RESUMED IN FILE 'REGISTRY' AT 15:05:48 ON 06 JUL 2006 FILE 'REGISTRY' ENTERED AT 15:05:48 ON 06 JUL 2006 COPYRIGHT (C) 2006 American Chemical Society (ACS)

COST IN U.S. DOLLARS FULL ESTIMATED COST	SINCE FILE ENTRY 334.76	TOTAL SESSION 766.46
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE => file reg	0.00	-8.25
COST IN U.S. DOLLARS FULL ESTIMATED COST	SINCE FILE ENTRY 334.76	TOTAL SESSION 766.46
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
CA SUBSCRIBER PRICE	ENTRY 0.00	SESSION -8.25

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http://www.cas.org/ONLINE/UG/regprops.html

Uploading C:\Program Files\Stnexp\Queries\10530627d.str

L21 STRUCTURE UPLOADED

=> d 121

L21 HAS NO ANSWERS L21 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s 121 sss sam

SAMPLE SEARCH INITIATED 15:06:20 FILE 'REGISTRY' SAMPLE SCREEN SEARCH COMPLETED -712 TO ITERATE

100.0% PROCESSED

712 ITERATIONS

8 ANSWERS

SEARCH TIME: 00.00.02

FULL FILE PROJECTIONS: ONLINE **COMPLETE** BATCH **COMPLETE**

PROJECTED ITERATIONS: PROJECTED ANSWERS:

12640 TO 15840 8 TO 329

L22 8 SEA SSS SAM L21

=> s 121 sss full

FULL SEARCH INITIATED 15:06:31 FILE 'REGISTRY' FULL SCREEN SEARCH COMPLETED -14160 TO ITERATE

100.0% PROCESSED 14160 ITERATIONS SEARCH TIME: 00.00.01

178 ANSWERS

L23 178 SEA SSS FUL L21

=> d scan

REGISTRY COPYRIGHT 2006 ACS on STN L23 178 ANSWERS

9H-Purin-6-aminium, 9-β-D-arabinofuranosyl-N,N,N-trimethyl- (9CI)

MF C13 H20 N5 O4

CI COM

Absolute stereochemistry.

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):10

REGISTRY COPYRIGHT 2006 ACS on STN L23 178 ANSWERS

IN 6H-Purin-6-one, 1,9-dihydro-9-(2-C-methyl- α -D-ribofuranosyl)-, oxime (9CI)

MF C11 H15 N5 O5

L23 178 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN IN Inosine-8-13C-1,7-15N2, O-methyloxime (9CI) MF C11 H15 N5 O5

Absolute stereochemistry.

L23 178 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN IN Adenosine, N-(2-aminoethyl)-2'-C-(trifluoromethyl)- (9CI) MF C13 H17 F3 N6 O4

L23 178 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN IN Adenosine, 2'-C-cyclopropyl-N-methyl- (9CI) MF C14 H19 N5 O4

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L23 178 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN IN Adenosine, 4'-C-ethyl-N,N-dimethyl- (9CI) MF C14 H21 N5 O4

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L23 178 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN IN Adenosine, 2'-C-ethyl-N,N-dimethyl- (9CI) MF C14 H21 N5 O4

L23 178 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN IN Adenosine, N-(2-aminoethyl)-2'-C-methyl- (9CI) MF C13 H20 N6 O4

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L23 178 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN

IN Rhodium(2+), di- μ -hydroxybis(N-methyladenosine- κ N7)bis[(1,2,3,4,5- η)-1,2,3,4,5-pentamethyl-2,4-cyclopentadien-1-yl]di-, stereoisomer, salt with trifluoromethanesulfonic acid (1:2), trihydrate (9CI)

MF C42 H62 N10 O10 Rh2 . C F3 O3 S . 3 H2 O

CM 1

CM 2

PAGE 1-A

PAGE 2-A

CM 3

L23 178 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN

IN Tungsten, pentacarbonyl (N-methyladenosine-κN1)-, (OC-6-22)- (9CI)

MF C16 H15 N5 O9 W

CI CCS

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> file caplus COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION FULL ESTIMATED COST 167.82 934.28 SINCE FILE DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) TOTAL ENTRY SESSION CA SUBSCRIBER PRICE 0.00 -8.25

FILE 'CAPLUS' ENTERED AT 15:07:41 ON 06 JUL 2006 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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(FILE 'HOME' ENTERED AT 13:50:33 ON 06 JUL 2006)

FILE 'REGISTRY' ENTERED AT 13:50:41 ON 06 JUL 2006

L1STRUCTURE UPLOADED L2 3 S L1 SSS SAM L3 104 S L1 SSS FULL FILE 'CAPLUS' ENTERED AT 13:51:24 ON 06 JUL 2006 L455 S L3 FILE 'REGISTRY' ENTERED AT 14:29:47 ON 06 JUL 2006 L5 STRUCTURE UPLOADED L6 0 S L5 SSS SAM L7 0 S L5 FULL FILE 'CAPLUS' ENTERED AT 14:30:42 ON 06 JUL 2006 L8 0 S 200362256.PN L9 0 S 200362256/PN L10 1 S WO 200362256/PN SEL RN FILE 'REGISTRY' ENTERED AT 14:33:21 ON 06 JUL 2006 L1139 S E1-E39 FILE 'CAPLUS' ENTERED AT 14:36:34 ON 06 JUL 2006 FILE 'HCAPLUS' ENTERED AT 14:36:57 ON 06 JUL 2006 FILE 'REGISTRY' ENTERED AT 14:45:20 ON 06 JUL 2006 E 1068-57-1/RN L12 1 S E3 L13 1 S 565435-03-2/RN L141 S 565435-04-3/RN FILE 'CAPLUS' ENTERED AT 14:48:03 ON 06 JUL 2006 L15 2 S L13 OR L14 FILE 'REGISTRY' ENTERED AT 14:53:10 ON 06 JUL 2006 L16 STRUCTURE UPLOADED L17 0 S L16 SSS SAM 0 S L16 FULL L18 L19 STRUCTURE UPLOADED L20 0 S L19 FULL FILE 'REGISTRY' ENTERED AT 15:05:56 ON 06 JUL 2006 L21 STRUCTURE UPLOADED L22 8 S L21 SSS SAM L23 178 S L21 SSS FULL FILE 'CAPLUS' ENTERED AT 15:07:41 ON 06 JUL 2006 => s 123 L24 888 L23 => file req COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION FULL ESTIMATED COST 2.30 936.58 DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION CA SUBSCRIBER PRICE -8.25 0.00

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 5 JUL 2006 HIGHEST RN 890705-10-9 DICTIONARY FILE UPDATES: 5 JUL 2006 HIGHEST RN 890705-10-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

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Uploading C:\Program Files\Stnexp\Queries\10530627e.str

L25 STRUCTURE UPLOADED

=> s 125 sss sam

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SAMPLE SCREEN SEARCH COMPLETED - 26 TO ITERATE

100.0% PROCESSED 26 ITERATIONS 0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 215 TO 825

PROJECTED ANSWERS: 0 TO 0

L26 0 SEA SSS SAM L25

=> s 125 full

FULL SEARCH INITIATED 15:11:03 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 443 TO ITERATE

100.0% PROCESSED 443 ITERATIONS 24 ANSWERS

SEARCH TIME: 00.00.01

L27 24 SEA SSS FUL L25

=> file caplus

COST IN U.S. DOLLARS
SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST
166.94
1103.52

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL

CA SUBSCRIBER PRICE ENTRY SESSION 0.00 -8.25

FILE 'CAPLUS' ENTERED AT 15:11:09 ON 06 JUL 2006 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 6 Jul 2006 VOL 145 ISS 2 FILE LAST UPDATED: 5 Jul 2006 (20060705/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

=> s 127

L28 11 L27

=> d bib abs hitstr 1-11 128

ANSWER 1 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2005:559568 CAPLUS

DN 143:230125

Antitumor Activity of C-Methyl-β-D-ribofuranosyladenine Nucleoside ΤI Ribonucleotide Reductase Inhibitors

ΑU Franchetti, Palmarisa; Cappellacci, Loredana; Pasqualini, Michela; Petrelli, Riccardo; Vita, Patrizia; Jayaram, Hiremagalur N.; Horvath, Zsuzsanna; Szekeres, Thomas; Grifantin, Mario

CS Dipartimento di Scienze Chimiche, Unifersita di Camerino, Camerino, 62032, Italy

SO Journal of Medicinal Chemistry (2)005, 48(15), 4983-4989 CODEN: JMCMAR; ISSN: 0022-2623

PΒ American Chemical Society

DT Journal

LA English

os CASREACT 143:230125

AΒ A series of adenosine derivs. substituted at the 1'-, 2'-, or 3'-position of the ribose ring with a Me group was synthesized and evaluated for antitumor activity. From this study 3'-C-methyladenosine (3'-Me-Ado) emerged as the most active compound, showing activity against human myelogenous leukemia K562, myltidrug resistant human leukemia K562IU, human promyelocytic leukemia/HL-60, human colon carcinoma HT-29, and human breast carcinoma MCF-7 cell/lines with IC50 values ranging from 11 to 38 μM. Structure-activity rel/ationship studies showed that the structure of 3'-Me-Ado is crucial fo ${\not t}$ the activity. Substitution of a hydrogen atom of the N6-amino group with a small alkyl or cycloalkyl group, the introduction of a chlorine atom in the 2-position of the purine ring, or the moving of the Me group from the 3'-position to other ribose positions brought about a decrease or loss of antitumor activity. The antiproliferative activity of 3'-Me-Ado appears to be related to its ability to deplete both intracellular purine and pyrimidine deoxynucleotides through ribonucleotide reductase inhibition.

IT 565450-76-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation, structure-activity, and antitumor activity of C-methyl-β-D-ribofuranosyladenine nucleoside ribonucleotide reductase inhibitors)

RN 565450-76-2 CAPLUS

CN Adenosine, N-methyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD

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ALL CITATIONS AVAILABLE IN THE RE FORMAT
     ANSWER 2 OF 11 CAPLUS COPYRIGHT 2006 ACS
L28
                                                    on STN
     2005:74688 CAPLUS
AN
DN
     142:336573
     Synthesis of 9-(2-\beta-C-methyl-\beta-D-ribofyranosyl)-6-substituted
TI
     purine derivatives as inhibitors of HQV RNA replication
     Ding, Yili; Girardet, Jean-Luc; Hong/Zhi; Lai, Vicky C. H.; An, Haoyun;
ΑU
     Koh, Yung-hyo; Shaw, Stephanie Z.; Zhong, Weidong
CS
     Valeant Pharmaceuticals International, Costa Mesa, CA, 92626, USA
so
     Bioorganic & Medicinal Chemistry Letters (20) (5), 15(3), 709-713
     CODEN: BMCLE8; ISSN: 0960-894X
PΒ
     Elsevier B.V.
DT
     Journal
LA
     English
     A series of 9-(2'-\beta-C-methyl-\beta-D-ribofuranosyl)-6-substituted
AB
     purine derivs. were synthesized as potential inhibitors of HCV RNA
     replication. Their inhibitory activities in a cell based HCV replicon
     assay were reported. A prodrug approach was used to further improve the
     potency of these compds. By increasing the intracellular levels of 5'-monophosphate metabolites. These nucleotide prodrugs showed much
     improved inhibitory activities of HCV RNA replication.
     565435-08-7P 565435-18-9P 565435-19-0P
     565435-22-5P 565435-24 7P 565450-76-2P
     565450-77-3P 728022-80/8P
     RL: BSU (Biological study, unclassified); SPN (Synthetic preparation);
     BIOL (Biological study); PREP (Preparation)
         (synthesis of 9-(\frac{1}{2}-\beta-C-methyl-\beta-D-ribofuranosyl)-6-
        substituted purine derivs. as inhibitors of HCV RNA replication)
RN
     565435-08-7 CAPLUS
CN
     Adenosine, N-(2-hydroxyethyl)-2'-C-methyl- (9CI) (CA INDEX NAME)
Absolute stereochemistry
HO.
           NH
                                     OH
                          R
                          R
                     Me
```

OH

OH

RN 565435-18-9 CAPLUS CN Inosine, 2'-C-methyl-, oxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 565435-19-0 CAPLUS
CN Adenosine, N-methoxy-N-methyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 565435-22-5 CAPLUS CN Adenosine, N-(2-aminoethyl)-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 565435-24-7 CAPLUS CN Inosine, 2'-C-methyl-, O-methyloxime (9CI) (CA INDEX NAME)

RN 565450-76-2 CAPLUS

CN Adenosine, N-methyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 565450-77-3 CAPLUS

CN Adenosine, N, N-dimethyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 728022-80-8 CAPLUS

CN Adenosine, N-hydroxy-N-methyl-2'-C-methyl- (9CI) (CA INDEX NAME)

RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
L28
     ANSWER 3 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
     2004:633938 CAPLUS
AN
DN
     141:157387
     Synthesis and use of 2'-substituted-N6-modified nucleosides as antiviral
TI
     agents
     An, Haoyun; Ramasamy, Kanda; Shaw, Stephanie
IN
                                           Bal Leite
PA
     Ribapharm Inc., USA
     PCT Int. Appl., 25 pp.
so
     CODEN: PIXXD2
DT
     Patent
     English
LA
FAN.CNT 1
     PATENT NO.
                         KIND
                                DATE
                                            APPLICATION NO.
                                                                    DATE
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ΡI
     WO 2004065398
                          A2
                                 20040805
                                            WO 2004-US1125
                                                                    20040115
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             <del>LK, L</del>R, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI
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                                           US 2006-542235
                                                                    20060123
PRAI 0S 2003-440666P
                          Р
                                2003Ø115
     WO 2004-US1125
                                2004/0115
                          W
                                                 Do ODP
os
     CASREACT 141:157387; MARPAT 141:157387
GΙ
```

Ι

AB An improved method of preparing a sugar modified nucleoside analog I, wherein R is selected from the group consisting of NH2NH2, N(CH3)NH2, N(CH3)OH, NHOH, NHOCH3, NHOCH2CH3, NHN(CH3)2, N(CH3)NHCH3, NHNHCH3, NHNHCH3, and NHNHCOOCH3, includes a protocol in which a hydroxy

group of a sugar is selectively deprotected and oxidized prior to nucleophilic modification of the corresponding carbonyl group. The modified sugar is then coupled to a heterocyclic base that is modified with a dual nucleophilic reagent in a further step that provides N6-modified adenosine analogs with high stereoselectivity. Contemplated antiviral and immunomodulatory activities of title nucleosides are reported (no data). Thus, I [R = N(Me)NH2] was prepared from 2-iodo-benzoic acid via stereoselective glycosylation with 6-chloropurine. IT 565435-14-5P 565435-18-9P 565435-24-7P 728022-80-8P RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (synthesis and use of 2'-substituted-N6-modified nucleosides as antiviral agents via stereoselective glycosylation) RN 565435-14-5 CAPLUS 9H-Purine, 6-(1-methylhydrazino)-9-(2-C-methyl-β-D-ribofuranosyl)-CN (CA INDEX NAME)

Absolute stereochemistry.

RN 565435-18-9 CAPLUS
CN Inosine, 2'-C-methyl-, oxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 565435-24-7 CAPLUS CN Inosine, 2'-C-methyl-, O-methyloxime (9CI) (CA INDEX NAME)

RN 728022-80-8 CAPLUS

CN Adenosine, N-hydroxy-N-methyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

```
L28
     ANSWER 4 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ΑN
     2004:566635 CAPLUS
DN
     141:89323
     Process for the production of 3'-nucleoside prodrugs
ΤI
     Storer, Richard; Moussa, Adel; Mathieu, Steven; Qu, Lin
IN
PA
     Idenix Cayman Limited, Cayman I.
     PCT Int. Appl., 57 pp.
so
     CODEN: PIXXD2
DT
     Patent
     English
LA
FAN.CNT 1
     PATENT NO.
                         KIND
                                 DATE
                                             APPLICATION NO.
                                                                     DATE
PΙ
     WO 2004058792
                                 20040715
                                             WO 2003-US41603
                          Α1
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                          A1
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IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

	BR 2003016868	Α	20051 Ø 25	BR	2003-16868	20031223
	CN 1751058	Α	20060ß22	CN	2003-80109820	20031223
	JP 2006514038	T2	2006 427	JP	2004-562599	20031223
	NO 2005003557	Α	2005 / 908	NO	2005-3557	20050720
PRAI	US 2002-436150P	P	2002 / 1223			
	WO 2003-US41603	W	20031223			
os	CASREACT 141:89323;	MARPAT	141:89323			
GI						

AB Provided is a single-step process for the regioselective 3'-acylation of a ribofuranosyl 2'- or 3'-branched nucleosides I, wherein B is nucleobase. These compds. are useful as antiviral agents, and in particular, can be used to treat Flaviviridae infections in a host in need thereof (no data). Thus, 9-(2'-C-methyl-3'-O-valinoyl- β -D-ribofuranosyl)-6-N-methyladenine dihydrochloride was prepared via regioselective esterification of 9-(2'-C-methyl- β -D-ribofuranosyl)-6-N-methyladenine with N-(tert-butoxycarbonyl)-L-valine.

IT 565450-76-2

RL: RCT (Reactant); RACT (Reactant or reagent)
 (process for production of nucleoside prodrugs via regioselective
 esterification)

RN 565450-76-2 CAPLUS

CN Adenosine, N-methyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L28 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:453348 CAPLUS

DN 141:17578

TI Treatment of Flaviviridae infection with 2'-branched nucleosides and another mutation-inducing drug such as interferon

IN Sommadossi, Jean-Pierre; La Colla, Paolo; Standring, David; Bichko, Vadim; Qu, Lin

PA Idenix (Cayman) Limited, Cayman I.; Universita Degli Studi Di Cagliari

SO PCT Int. Appl., 166 pp.

CODEN: PIXXD2

DT Patent

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LΑ
     English
FAN.CNT 1
     PATENT NO.
                          KIND
                                  DATE
                                              APPLICATION NO.
                                                                      DATE
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     WO 2004046331
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     NO 2005002920
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                                              NO 2005-2920
                                                                      20050615
PRAI US 2002-426675P
                           Р
                                 20021115
                                 20031117
     WO 2003-US36714
                           W
os
     MARPAT 141:17578
AB
     The present invention discloses a method for the treatment of Flaviviridae
     infection that includes the administration of a 2'-branched nucleoside, or
     a pharmaceutically acceptable prodrug and/or salt thereof, to a human in
     need of therapy in combination or alternation with a drug that directly or
     indirectly induces a mutation in the viral genome at a location other than
     a mutation of a nucleotide that results in a change from serine to a
```

The present invention discloses a method for the treatment of Flaviviridae infection that includes the administration of a 2'-branched nucleoside, or a pharmaceutically acceptable prodrug and/or salt thereof, to a human in need of therapy in combination or alternation with a drug that directly or indirectly induces a mutation in the viral genome at a location other than a mutation of a nucleotide that results in a change from serine to a different amino acid in the highly conserved consensus sequence, XRX<u>S</u>GXXXT, of domain B of the RNA polymerase region, or is associated with such a mutation. The invention also includes a method to detect a mutant strain of Flaviviridae and a method for its treatment. Thus, in bovine viral diarrhea virus (BVDV)-infected MDBK cells treated with β -D-2'-methylcytidine, viruses resistant to the nucleoside appeared. The drug resistance was associated with a mutation in the NS5B gene which resulted in an S405T substitution in the encoded RNA-dependent RNA polymerase. These mutant viruses were sensitive to Intron A (interferon α -2b). Intron A and β -D-2'-methylcytidine exhibited synergistic inhibitory activity on BVDV growth in MDBK cells.

IT 565450-76-2

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(treatment of Flaviviridae infection with 2'-branched nucleosides and another mutation-inducing drug such as interferon)

RN 565450-76-2 CAPLUS

CN Adenosine, N-methyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

 \int

```
ANSWER 6 OF 11 CAPLUS
                              COPYRIGHT 2006 ACS on STN
L28
     2004:290484 CAPLUS
AN
DN
     140:327061
     Nucleoside derivatives for treating hepatitis C virus infection
TI
IN
     Roberts, Christopher Don; Dyatkina, Natalia B.
PA
     Genelabs Technologies, Inc., USA
SO
     PCT Int. Appl., 119 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 2
     PATENT NO.
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                                  DATE
                                              APPLICATION NO.
                                                                      DATE
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PΙ
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             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
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             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
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                                                                      20030930
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                                              AU 2003-279797
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     EP 1572097
                           A3
                                  20051207
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
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     JP 2006505537
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                                  20050524
                                              NO 2005-1969
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PRAI US 2002-415222P
                           P
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     US 2003-443169P
                           P
                                  2003,0129
                                  20030930
     WO 2003-US31433
                           W
os
     MARPAT 140:327061
AΒ
     Nucleoside compns. and methods for treating hepatitis C virus infections.
     Thus, 9-(2'-C-methyl-\beta-D-ribofuranosyl)-6-methoxyaminopurine was
     prepared by the reaction of 6-chloro-9-(2'-C-methyl-\beta-D-
     ribofuranosyl) purine and methxylamine. This compound exhibited
     anti-hepatitis C activity by inhibiting HCV polymerase.
     565435-18-9P 677298-62-3P
IT
     RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); RACT (Reactant or reagent); USES (Uses)
        (nucleoside derivs. for treating hepatitis C virus infection)
RN
     565435-18-9 CAPLUS
CN
     Inosine, 2'-C-methyl-, oxime (9CI) (CA INDEX NAME)
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RN 677298-62-3 CAPLUS

CN 6H-Purin-6-one, 1,9-dihydro-9-(2-C-methyl- α -D-ribofuranosyl)-, oxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 565435-24-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(nucleoside derivs. for treating hepatitis C virus infection)

RN 565435-24-7 CAPLUS

CN Inosine, 2'-C-methyl-, O-methyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.

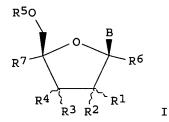
L28 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:2898 CAPLUS

DN 140:42424

TI Preparation of nucleoside derivatives as inhibitors of RNA-dependent RNA

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viral polymerase
IN
     Carroll, Steven S.; Olsen, David B.; Durette, Philippe L.; Bhat,
     Balkrishen; Dande, Prasad; Eldrup, Anne B.
PA
     Merck & Co., Inc., USA; Isis Pharmaceuticals, Inc.
     PCT Int. Appl., 43 pp.
SO
     CODEN: PIXXD2
DT
     Patent
     English
T.A
FAN.CNT 1
                                 DATE
     PATENT NO.
                          KIND
                                             APPLICATION NO.
                                                                      DATE
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ΡI
     WO 2004000858
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     WO 2004000858
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PRAI US 2002-390579P
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     WO 2003-US19172
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                                 20030617
os
     MARPAT 140:42424
GΙ
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AΒ The present invention provides nucleoside compds. I, wherein B is nucleobase; R1 is fluoromethyl, difluoromethyl, trifluoromethyl; R2 is H, F, amino, OH, SH, alkoxy, alkylcarbonyloxy, alkyl; R3 and R4 are independently H, Cn, N3, halogen, OH, SH, amino, alkoxy, alkylcarconyloxy, alkenyl, alkynyl; R5 is H, alkylcarbonyl, P3O9H4, P2O6H3, phosphophonyl; R6 and R7 independently H, Me, hydroxymethyl, fluoromethyl; and certain derivs. thereof which are inhibitors of RNA-dependent RNA viral polymerase. These compds. are inhibitors of RNA-dependent RNA viral replication and are useful for the treatment of RNA-dependent RNA viral infection. They are particularly useful as inhibitors of hepatitis C virus (HCV) NS5B polymerase, as inhibitors of HCV replication, and/or for the treatment of hepatitis C infection. The invention also describes pharmaceutical compns. containing such nucleoside compds. alone or in combination with other agents active against RNA-dependent RNA viral infection, in particular HCV infection. Also disclosed are methods of inhibiting RNA-dependent RNA polymerase, inhibiting RNA-dependent RNA

viral replication, and/or treating RNA-dependent RNA viral infection with the nucleoside compds. of the present invention. Thus, 2-amino-9-(2-C-fluoromethyl-β-D-ribofuranosyl)-3,9-dihydropurin-6-one was prepared and tested as inhibitor of RNA-dependent RNA viral polymerase. Title compds. tested in the HCV NS5B polymerase assay exhibited IC50's less than 100 µmol. 636581-90-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(preparation of nucleoside derivs. as inhibitors of RNA-dependent RNA viral polymerase)

RN 636581-90-3 CAPLUS

IT

CN Adenosine, 2'-C-(fluoromethyl)-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L28 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

2003:892793 CAPLUS AN

DN 139:365176

TI Preparation of nucleoside derivatives for treating hepatitis C virus infection

IN Roberts, Christopher Don; Dyatkina, Natalia B.; Keicher, Jesse D.; Liehr, Sebastian Johannes Reinhard; Hanson, Eric Jason

PA Genelabs Technologies, Inc., USA

so PCT Int. Appl., 182 pp.

CODEN: PIXXD2

DTPatent

LΑ English

FAN.	CNT	1																
	PAT	ENT 1	NO.					DATE			APPL	ICAT	ION	NO.		D	ATE	
DT	WO 00000000			30 00001110														
ΡI	WO 2003093290							WO 2003-US14237						20030506				
	WO 2003093290																	
	WO 2003093290			C1	2005ø519													
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			LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,
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	AU 2003232071			A1	20031/117			AU 2003-232071						20030506				
•	US 2004063658				Al				US 2003-431631						20030506			
EP 1501850				A2				EP 2003-747674										

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AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK BR 2003009581 Α 2005032*9* BR 2003-9581 20030506 CN 1653077 Α 20050810 CN 2003-810239 20030506 JP 2005530759 **T2** 200510/13 JP 2004-501429 20030506 NO 2004005247 Α 200411/30 NO 2004-5247 20041130 Р PRAI US 2002-378624P 20020/506 P 20020628 US 2002-392871P WO 2003-US14237 2003/0506 OS MARPAT 139:365176 GI

AB Nucleosides I-III, wherein R and R1 are independently H, alkyl, alkenyl, alkynyl, provided that R and R1 are not both H; R2 is alkyl, cycloalkyl, alkenyl, alkynyl, acylamino, guanidino, amidino, thioacylamino, OH, alkoxy, halo, nitro, aryl, heteroaryl, substituted amine; W is H, phosphate, phosphonate, acyl, alkyl, sulfonate, lipid, amino acid, sugar residue, peptide, cholesterol; X is H, halo, alkyl, substituted amine; Y is H, halo, OH, alkylthio, substituted amine; Z is H, halo, OH, alkyl, substituted amine; T is nucleobase, were prepared as HCV RNA polymerase inhibitors and for treating hepatitis C virus infections. Thus, 2-(4-amino-pyrrolo[3,2-c]pyridin-1-yl)-5-hydroxymethyl-3-methyltetrahydrofuran-3,4-diol was prepared for treating hepatitis C virus infections (no data). Different kind of formulation such as tablet, capsule, suspension, injectable, and suppository formulation are reported.

IT 565435-18-9P 565435-22-5P 565435-24-7P 622380-55-6P 622380-68-1P 622380-73-8P 622380-77-2P

RN

CN

RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of nucleoside derivs. for treating hepatitis C virus infection) 565435-18-9 CAPLUS

Inosine, 2'-C-methyl-, oxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 565435-22-5 CAPLUS CN Adenosine, N-(2-aminoethyl)-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 565435-24-7 CAPLUS CN Inosine, 2'-C-methyl-, O-methyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 622380-55-6 CAPLUS
CN Adenosine, N-[2-amino-1-(3H-indol-3-ylmethyl)-2-oxoethyl]-2'-C-methyl(9CI) (CA INDEX NAME)

RN 622380-68-1 CAPLUS

CN Adenosine, N-(2-aminoethyl)-2'-C-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 622380-73-8 CAPLUS

CN Adenosine, N-(2-aminoethyl)-2'-C-ethenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 622380-77-2 CAPLUS

CN Adenosine, N-(2-aminoethyl)-2'-C-ethynyl- (9CI) (CA INDEX NAME)

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L28
     ANSWER 9 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
AN
     2003:591196
                 CAPLUS
DN
     139:133790
ΤI
     Preparation of 2'-β-modified-6-substituted adenosine analogs and
     their use as antiviral agents
IN
     An, Haoyun; Ding, Yili; Shaw, Stephanie; Hong, Zhi
PA
     Ribapharm Inc., USA
     PCT Int. Appl., 45 pp.
so
     CODEN: PIXXD2
                                            Mm
DT
     Patent
LA
     English
FAN.CNT 4
     PATENT NO.
                         KIND
                                DATE
                                            APPLICATION NO.
                                                                   DATE
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ΡI
     WO 2003062256
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             CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                20020117
PRAI US 2002-350296P
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    MARPAT 139:133790
GΙ
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AΒ

Ι

selected from the group consisting of an alkyl, an O-alkyl, an alkenyl, an alkynyl, and CN, wherein the alkyl, the alkenyl, or the alkynyl is optionally substituted with a halogen or OH; A is CH or N, and E is C-R6 or N, such that (1) when A is CH then E is C-R6 or N, and (2) when A is N then E is CH; X is NR1R2, NR2NR3R4, NR2N=NR3, NR2N=CHR3, NR2N=O, NR2C(=0)NR3R4, NR2C(=S)NR3R4, NR2C(=NH)NR3R4, NR1C(=0)NR2NR3R4, NR2OR3, ONHC(O)O-alkyl, ONHC(O)O-aryl, ONR3R4, SNR1R2, SONR1R2, or S(O)2NR1R2; wherein R1-R4 are independently H, alkyl, substituted alkyl, O-alkyl, cyclic alkyl, heterocyclic alkyl, alkoxy, alkaryl, aryl, heterocyclic aryl, substituted aryl, acyl, substituted acyl, S(0)2-alkyl, NO, NH2, or OH; and R6 is H, NH2, halogen, N3, NHR1, NHCOR1 NR1R2, NHSO2R1, NHCONHR1, NHCSNHR1, CH2NHR1, CHR1NHR2, NHNH2, CN, alkyl, alkenyl, alkynyl, CH2-aryl, CH2-heterocycle, halogen, OH, or SH; are prepared by conventional and combinatorial library approaches. Contemplated compds. are particularly useful as therapeutic agents, and especially as antiviral agents. Thus, N6-[3-(methylthio)phenyl]-9H-(2'- β -C-methyl- β -D-

ribofuranosyl) adenine was prepared and tested in vitro as antiviral agent against influenza virus A, bovine viral diarrhea virus, Hepatitis B virus, HIV-1 virus and human Rhinovirus.

IT 565435-08-7P 565435-12-3P 565435-14-5P 565435-18-9P 565435-19-0P 565435-22-5P

RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)

(preparation of 2'- β -modified-6-substituted adenosine analogs and their use as antiviral agents)

RN 565435-08-7 CAPLUS

CN Adenosine, N-(2-hydroxyethyl)-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 565435-12-3 CAPLUS
CN Ethanol, 2-[1-[9-(2-C-methyl-β-D-ribofuranosyl)-9H-purin-6yl]hydrazino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 565435-18-9 CAPLUS
CN Inosine, 2'-C-methyl-, oxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 565435-19-0 CAPLUS CN Adenosine, N-methoxy-N-methyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 565435-22-5 CAPLUS CN Adenosine, N-(2-aminoethyl)-2'-C-methyl- (9CI) (CA INDEX NAME)

IT 565435-24-7

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of 2'- β -modified-6-substituted adenosine analogs and their use as antiviral agents)

RN 565435-24-7 CAPLUS

CN Inosine, 2'-C-methyl-, O-methyloxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2003:591195 CAPLUS

DN 139:133789

TI Preparation of sugar modified nucleosides as antiviral agents

IN Hong, Zhi; An, Haoyun; Ding, Yili; Girardet, Jean-luc; Zhong, Weidong

PA Ribapharm Inc., USA

SO PCT Int. Appl., 33 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 4

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CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG EP 1572705 A2 20050914 EP 2002-776103 20021002 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK 20020117 PRAI US 2002-350296P Ρ P 20020626 US 2002-391800P WO 2002-US31556 W 20021002 os MARPAT 139:133789 GΙ

AB Various 2'-modified nucleoside analogs I and II wherein X is NH2, NHMe, NMe2, OMe, SMe, and corresponding prodrugs are provided, and particularly contemplated methods of use include use as antiviral agents, and especially as antiviral agents against HCV.

IT 565450-72-8P 565450-73-9P 565450-76-2P

565450-77-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of sugar modified nucleosides as antiviral agents)

RN 565450-72-8 CAPLUS

CN Adenosine, 2'-C-ethyl-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 565450-73-9 CAPLUS

CN Adenosine, 2'-C-ethyl-N,N-dimethyl- (9CI) (CA INDEX NAME)

RN 565450-76-2 CAPLUS
CN Adenosine, N-methyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 565450-77-3 CAPLUS
CN Adenosine, N,N-dimethyl-2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 565450-99-9 CAPLUS

CN Adenosine, 2'-C-ethenyl-N, N-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 565451-03-8 CAPLUS

CN Adenosine, 2'-C-cyclopropyl-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 565451-04-9 CAPLUS

CN Adenosine, 2'-C-cyclopropyl-N, N-dimethyl- (9CI) (CA INDEX NAME)

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L28 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
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AN 1969:502192 CAPLUS

DN 71:102192

TI Substituted purine nucleosides

IN Walton, Edward

PA Merck and Co., Inc.

SO Fr., 11 pp.

CODEN: FRXXAK

DT Patent

LA French

FAN.CNT 1

FAN.CNT 1				
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI FR 1521076		19680412	FR 1967-104388	19670427
DE 1593110			DE	
DE 1620053			DE	
DE 1695411			DE	
DE 1768470			DE	
DE 1770700			DE	
GB 1163102			GB	
GB 1187824			GB	
GB 1187825			GB	
US 3480613		19691125	US	19670703
PRAI US		19660502		

The title compds. (I), which were useful in preparing nucleotides for the study of nucleic acid metabolism were prepared by treating 2,6-substituted chloromercuri-purines with 2,3,5,-tri-O-acyl-2-methyl-D-ribofuranosyl halides to give 2,6-substituted 9-(2,3,5,-tri-O-acyl-2-C-methyl-Dribofuranosyl) purines which were solvolyzed, aminolyzed, or mercaptolyzed. Thus, a solution of 5 g. 2-C-methyl-D-ribono-1,4-lactone in 100 cc. dry pyridine at 5° was treated with 17 cc.BzCl, heated 65-70° 4 hrs., and kept at room temperature 6 hrs. to give 60% 2,3,5-tri-O-benzoyl-2-C-methyl-D-ribono-1,4-lactone (II) m. 138-40°. A solution 7 g. II in 30 cc. dry tetrahydrofuran under N was cooled and treated with 58.8 cc. M di-sec-isoamyl-borane, kept at room temperature 16 hrs., 6 cc. H2O added, refluxed 0.5 hr., and at 5°, 11.5 cc. H2O2 added keeping the pH 7-8 by the addition of about 7 cc. 3N Na2CO3 to give 37% 2,3,5-tri-O-benzoyl-2-C-methyl-(α and β)-Dribofuranose (III) purified by chromatog. on silica gel. A solution 4.2 q. III (containing a small amount of 3,5-di-O-benzoyl-2-C-methyl-(α , β)-Dribofuranose) in 80 cc. dry pyridine was treated with 8.0 cc. BzCl and heated at 90° for 4 hrs. to give 42% 1,2,3,5-tetra-O-benzoyl-2-Cmethyl- β -D-ribofuranose (IV), m. 155-6°, and 57% 1,2,3,5-tetra-O-benzoyl-2-C-methyl- α -D-ribofuranose (V) as an oil. to 100 cc. of a saturated HCl Et2O solution was added 2 cc. AcCl and 1.5 g. IV and the mixture kept at room temperature 2 hrs. to give

2,3,5-tri-O-benzoyl-2-C methyl-β-D-ribofuranosyl chloride (VI). A solution of 1.5 g. V in 7.5
 cc. AcOH was treated with a solution of 0.25 cc. AcBr and 7.5 cc. 32% HBr in
 AcOH and the mixture kept at 25° 24 hrs. to give 2,3,5-tri-O-benzoyl-

2-C-methyl-β-D-ribofuranosyl bromide. From a suspension of 5.95 g.
2-acetamido-9-chloromercuri-6-hydroxypurine in 175 cc. xylene about 25 cc. of xylene was distilled to remove traces of H2O, the VI prepared from 8.1 g. IV in 25 cc. dry xylene was added, and the mixture stirred at 50-100° and refluxed 1 hr. to give 2-acetamido-9-(2,3,5-tri-O-benzoyl-2-methyl-D-ribofuranosyl)-6-hydroxypurine (VII). Similarly prepared were:
6-N-methyl-9-(2,3,5-tri-O-benzoyl-C-methyl-D-ribofuranosyl)benzamidopurine (VIII); 6-chloro-9-(2,3,5-tri-O-benzoyl-2-C-methyl-D-ribofuranosyl)purine (X); 2,6-dibenzamido-9-(2,3,5-tri-O-benzoyl-2-C-methyl-D-ribofuranosyl)purine (X); 6-methyl-9-(2,3,5-tri-O-benzoyl-2-C-methyl-D-ribofuranosyl)purine (XI); 6-benzamido-9-(2,3,5-tri-O-benzoyl-2-C-methyl-D-ribofuranosyl)purine (XII). A suspension of 1.0 g. IX in 25 cc. MeOH containing 6.5 g. Me2NH was heated 10 hrs. in a sealed tube at 100° and concentrated in vacuo and the residue dissolved in 25 cc. H2O, washed with

and treated with 2 g. Dowex II-X8 strongly basic anion-exchange resin to give I (R1 = Me2N, R = H). A mixture of 1.2 g. X in 12 cc. dry MeOH was treated with 97 mg. Na in 12 cc. MeOH and refluxed 3 hrs. to give I (R =R1 = NH2). A suspension of 1.25 g. IX and 307 mg. thiourea in 3 cc. EtOH was refluxed 40 min. to give 9-(2,3,5-tri-O-benzoyl-2-C-methyl-Dribofuranosyl)purine-6-thiol, (XIII). A suspension of 400 mg. XIII in 3.5 cc. MeOH was treated with a solution prepared from 19.5 mg. Na in 3.5 cc. dry MeOH and the mixture refluxed 3 hrs. to give I (R = H, R1 = SH). A mixture 1 g. IX, 8 g. MeNH2, and 25 g. MeOH was heated at 100° 10 hrs. in a sealed tube to give I(R = H, R1 = NHMe). A solution of 1 g. IX in 17 cc. dioxane, 80 mg. MgO, and 0.5 g. of 5% Pd on C was shaken 98 hrs. in a H atmospheric at 25° to give 9-(2,3,5-tri-O-benzoyl-2-C-methyl-Dribofuranosyl)purine (XIV). A solution 400 mg. XIV in 8 cc. dry MeOH was treated with a solution of 23 mg. Na in 8 cc. dry MeOH and refluxed 3 hrs. to give I(R = R1 = H). A suspension of 800 mg. VII in 8 cc. anhydrous MeOH was treated with a solution of 105 mg. Na in 8 cc. dry MeOH and the mixture refluxed 2 hrs. to give 9-(2-C-methyl-D-ribofuranosyl)guanine. A solution of 479 mg. IX in 20 cc. MeOH containing 2 g. NH3 was kept at 5° 20 hrs. to give I(R = H, R1 = C1). A suspension of 3.9 g. VIII in 40 cc. dry MeOH was treated with a solution prepared from 175 mg. Na in 40 cc. dry MeOH, and the mixture refluxed 3.5 hrs. to give I(R = H, R1 = MeNH). A solution of 2.0 g. IX in 30 cc. EtOH containing 12 cc. EtNH2 was heated in a sealed tube at 100° for 10 hrs. to give I(R = H, R1 = NHEt). A solution of 605 mg. IX in 30 cc. dry MeOH was treated with a solution prepared by saturating 20 cc. of a

0.1N NaOMe solution with MeSH, and the mixture refluxed 30 min. to give I(R=H,R1=SMe). A mixture of 590 mg. XI and 50 cc. dry MeOH was treated with a solution prepared from 23 mg. Na and 10 cc. dry MeOH, and the mixture refluxed

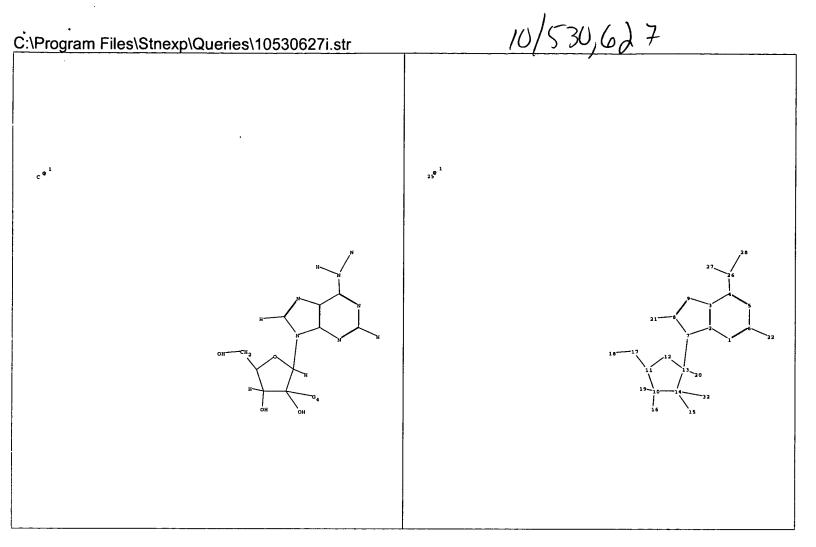
4 hrs. to give I(R = H, R1 = Me). A mixture 1.48 g. XII and 15 cc. MeOH was treated with a solution prepared from 70 mg. Na and 5 cc. MeOH, and the mixture refluxed 45 min. to give 59% 2'-C-methyladenosine.

IT 25899-60-9P 25899-63-2P

RN 25899-60-9 CAPLUS

CN Adenine, N,N-dimethyl-9-(2-C-methyl-D-ribofuranosyl)- (8CI) (CA INDEX NAME)

RN 25899-63-2 CAPLUS CN Adenine, N-methyl-9-(2-C-methyl-D-ribofuranosyl)- (8CI) (CA INDEX NAME)



chain nodes:

15 16 17 18 19 20 21 22 26 27 28 32

ring nodes:

1 2 3 4 5 6 7 8 9 10 11 12 13 14

ring/chain nodes:

29

chain bonds:

4-26 6-22 7-13 8-21 10-16 10-19 11-17 13-20 14-15 14-32 17-18 26-27 26-28 ring bonds :

1-2 1-6 2-3 2-7 3-4 3-9 4-5 5-6 7-8 8-9 10-11 10-14 11-12 12-13 13-14 exact/norm bonds :

2-7 3-9 4-26 7-8 7-13 8-9 10-11 10-14 10-16 11-12 12-13 13-14 14-15 14-32 26-28 exact bonds :

6-22 8-21 10-19 11-17 13-20 17-18 26-27

normalized bonds:

1-2 1-6 2-3 3-4 4-5 5-6

G1:CH3,NH2,H

G2:CH3,OH,MeO

G3:CN

G4:0,[*1]

Search For Mapent clasms
4+5 where 7 is:
C-or O-, both open
1 x is:

(B-N-NE(open)

Match level:

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:CLAS\$16:CLAS\$17:CLAS\$18:CLAS\$19:CLAS\$20:CLAS\$21:CLAS\$22:CLAS\$ 26:CLAS\$27:CLAS\$29:CLAS\$22:CLAS\$

=>

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L41 STRUCTURE UPLOADED

=> s 141 sss sam

SAMPLE SEARCH INITIATED 15:35:11 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 2 TO ITERATE

100.0% PROCESSED 2 ITERATIONS 0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**

PROJECTED ITERATIONS: 2 TO 124
PROJECTED ANSWERS: 0 TO 0

L42 0 SEA SSS SAM L41

=> s l41 sss full

FULL SEARCH INITIATED 15:35:19 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 17 TO ITERATE

100.0% PROCESSED 17 ITERATIONS 8 ANSWERS

SEARCH TIME: 00.00.02

L43 8 SEA SSS FUL L41

=> d 1-8 143

L43 ANSWER 1 OF 8 REGISTRY COPYRIGHT 2006 ACS on STN

RN 622380-62-5 REGISTRY

ED Entered STN: 01 Dec 2003

CN 3H-Indole-3-acetic acid, 2-[9-(2-C-methyl-β-D-ribofuranosyl)-9H-purin-6-yl]hydrazide (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C21 H23 N7 O5

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L43 ANSWER 2 OF 8 REGISTRY COPYRIGHT 2006 ACS on STN

RN 622379-60-6 REGISTRY

ED Entered STN: 01 Dec 2003

CN Inosine, 2'-C-methyl-, methylhydrazone (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C12 H18 N6 O4

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L43 ANSWER 3 OF 8 REGISTRY COPYRIGHT 2006 ACS on STN

RN 565435-17-8 REGISTRY

ED Entered STN: 13 Aug 2003

CN Methanesulfonic acid, 2-[9-(2-C-methyl-β-D-ribofuranosyl)-9H-purin-6yl]hydrazide (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C12 H18 N6 O6 S

SR CA

LC STN Files: CA, CAPLUS

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L43 ANSWER 4 OF 8 REGISTRY COPYRIGHT 2006 ACS on STN

RN 565435-16-7 REGISTRY

ED Entered STN: 13 Aug 2003

CN Acetic acid, 2-[9-(2-C-methyl- β -D-ribofuranosyl)-9H-purin-6-

yl]hydrazide (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C13 H18 N6 O5

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L43 ANSWER 5 OF 8 REGISTRY COPYRIGHT 2006 ACS on STN

RN 565435-15-6 REGISTRY

ED Entered STN: 13 Aug 2003

CN Hydrazinecarboxylic acid, 2-[9-(2-C-methyl- β -D-ribofuranosyl)-9H-

purin-6-yl]-, methyl ester (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C13 H18 N6 O6

SR CA

LC STN Files: CA, CAPLUS

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L43 ANSWER 6 OF 8 REGISTRY COPYRIGHT 2006 ACS on STN

RN 565435-13-4 REGISTRY

ED Entered STN: 13 Aug 2003

CN Inosine, 2'-C-methyl-, formylhydrazone (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C12 H16 N6 O5

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L43 ANSWER 7 OF 8 REGISTRY COPYRIGHT 2006 ACS on STN

RN 565435-11-2 REGISTRY

ED Entered STN: 13 Aug 2003

CN Inosine, 2'-C-methyl-, 2,2-dimethylhydrazone (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C13 H20 N6 O4

SR CA

LC STN Files: CA, CAPLUS

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L43 ANSWER 8 OF 8 REGISTRY COPYRIGHT 2006 ACS on STN

RN 565435-10-1 REGISTRY

ED Entered STN: 13 Aug 2003

CN Inosine, 2'-C-methyl-, hydrazone (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C11 H16 N6 O4

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION FULL ESTIMATED COST 182.58 1854.37 DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION CA SUBSCRIBER PRICE 0.00 -16.50

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=> s 143
L44
             2 L43
=> d bib abs hitstr 1-2
L44
     ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
AN
     2003:892793 CAPLUS
DN
     139:365176
     Preparation of nucleoside derivatives for treating hepatitis C virus
ΤI
     infection
IN
     Roberts, Christopher Don; Dyatkina, Natalia B.; Keicher, Jesse D.; Liehr,
     Sebastian Johannes Reinhard; Hanson, Eric Jason
PA
     Genelabs Technologies, Inc., USA
SO
     PCT Int. Appl., 182 pp.
     CODEN: PIXXD2
DT
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LΑ
     English
FAN.CNT 1
     PATENT NO.
                         KIND
                                DATE
                                            APPLICATION NO.
                                                                    DATE
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                                20031113
                                             WO 2003-US14237
                                                                    20030506
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                                20040318
     WO 2003093290
                          C1
                                20050519
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EP 1501850 A2 20050202 EP 2003-747674 20030506 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK BR 2003009581 Α 20050329 BR 2003-9581 20030506 CN 1653077 Α 20050810 CN 2003-810239 20030506 JP 2005530759 T2 20051013 JP 2004-501429 20030506 NO 2004005247 Α 20041130 NO 2004-5247 20041130 PRAI US 2002-378624P Р 20020506

20020628

20030506

WO 2003-US14237 OS MARPAT 139:365176

US 2002-392871P

Р

W

GI

AB Nucleosides I-III, wherein R and R1 are independently H, alkyl, alkenyl, alkynyl, provided that R and R1 are not both H; R2 is alkyl, cycloalkyl, alkenyl, alkynyl, acylamino, guanidino, amidino, thioacylamino, OH, alkoxy, halo, nitro, aryl, heteroaryl, substituted amine; W is H, phosphate, phosphonate, acyl, alkyl, sulfonate, lipid, amino acid, sugar residue, peptide, cholesterol; X is H, halo, alkyl, substituted amine; Y is H, halo, OH, alkylthio, substituted amine; Z is H, halo, OH, alkyl, substituted amine; T is nucleobase, were prepared as HCV RNA polymerase inhibitors and for treating hepatitis C virus infections. Thus, 2-(4-amino-pyrrolo[3,2-c]pyridin-1-yl)-5-hydroxymethyl-3-methyltetrahydrofuran-3,4-diol was prepared for treating hepatitis C virus infections (no data). Different kind of formulation such as tablet, capsule, suspension, injectable, and suppository formulation are reported.

IT 565435-10-1P 622379-60-6P 622380-62-5P

IT 565435-10-1P 622379-60-6P 622380-62-5P
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN
(Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
PREP (Preparation); USES (Uses)

(preparation of nucleoside derivs. for treating hepatitis C virus infection) 565435-10-1 CAPLUS

CN Inosine, 2'-C-methyl-, hydrazone (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN

RN 622379-60-6 CAPLUS Inosine, 2'-C-methyl-, methylhydrazone (9CI) (CA INDEX NAME) CN

Absolute stereochemistry.

RN622380-62-5 CAPLUS

CN 3H-Indole-3-acetic acid, 2-[9-(2-C-methyl-β-D-ribofuranosyl)-9H-purin-6-yl]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
L44
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AN 2003:591196 CAPLUS

DN 139:133790

Preparation of 2'-β-modified-6-substituted adenosine analogs and TItheir use as antiviral agents

IN An, Haoyun; Ding, Yili; Shaw, Stephanie; Hong, Zhi

PA Ribapharm Inc., USA

so PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 4

PATENT NO. DATE KIND APPLICATION NO. DATE -----------_ _ _ _ _ _ _ _ _ _ _ ------PΙ WO 2003062256 Α1 20030731 WO 2002-US34026 20021023 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG PRAI US 2002-350296P Р 20020117 MARPAT 139:133790

GI

os

Various 2'-beta-methyl-6-substituted adenosine analogs I in which Z is AB selected from the group consisting of an alkyl, an O-alkyl, an alkenyl, an alkynyl, and CN, wherein the alkyl, the alkenyl, or the alkynyl is optionally substituted with a halogen or OH; A is CH or N, and E is C-R6 or N, such that (1) when A is CH then E is C-R6 or N, and (2) when A is N then E is CH; X is NR1R2, NR2NR3R4, NR2N=NR3, NR2N=CHR3, NR2N=O, NR2C(=O)NR3R4, NR2C(=S)NR3R4, NR2C(=NH)NR3R4, NR1C(=O)NR2NR3R4, NR2OR3, ONHC(O)O-alkyl, ONHC(O)O-aryl, ONR3R4, SNR1R2, SONR1R2, or S(O)2NR1R2; wherein R1-R4 are independently H, alkyl, substituted alkyl, O-alkyl, cyclic alkyl, heterocyclic alkyl, alkoxy, alkaryl, aryl, heterocyclic aryl, substituted aryl, acyl, substituted acyl, S(O)2-alkyl, NO, NH2, or OH; and R6 is H, NH2, halogen, N3, NHR1, NHCOR1 NR1R2, NHSO2R1, NHCONHR1, NHCSNHR1, CH2NHR1, CHR1NHR2, NHNH2, CN, alkyl, alkenyl, alkynyl, CH2-aryl, CH2-heterocycle, halogen, OH, or SH; are prepared by conventional and combinatorial library approaches. Contemplated compds. are particularly useful as therapeutic agents, and especially as antiviral agents. Thus, N6-[3-(methylthio)phenyl]-9H-(2'- β -C-methyl- β -Dribofuranosyl)adenine was prepared and tested in vitro as antiviral agent against influenza virus A, bovine viral diarrhea virus, Hepatitis B virus, HIV-1 virus and human Rhinovirus.

IT 565435-10-1P 565435-11-2P 565435-13-4P 565435-15-6P 565435-16-7P 565435-17-8P

Ι

RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)

(preparation of 2'-β-modified-6-substituted adenosine analogs and their use as antiviral agents)

RN565435-10-1 CAPLUS

CNInosine, 2'-C-methyl-, hydrazone (9CI) (CA INDEX NAME)

$$R = R$$

$$OH$$

$$OH$$

RN 565435-11-2 CAPLUS

CN Inosine, 2'-C-methyl-, 2,2-dimethylhydrazone (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 565435-13-4 CAPLUS

CN Inosine, 2'-C-methyl-, formylhydrazone (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 565435-15-6 CAPLUS

CN Hydrazinecarboxylic acid, 2-[9-(2-C-methyl- β -D-ribofuranosyl)-9H-purin-6-yl]-, methyl ester (9CI) (CA INDEX NAME)

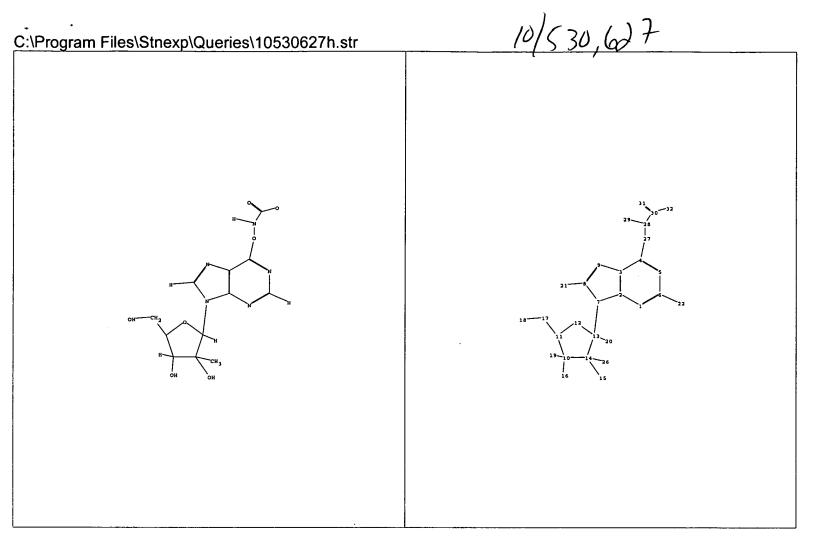
RN 565435-16-7 CAPLUS CN Acetic acid, 2-[9-(2-C-methyl- β -D-ribofuranosyl)-9H-purin-6-yl]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 565435-17-8 CAPLUS
CN Methanesulfonic acid, 2-[9-(2-C-methyl-β-D-ribofuranosyl)-9H-purin-6yl]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT



chain nodes:

15 16 17 18 19 20 21 22 26 27 28 29 30 31 32

ring nodes:

1 2 3 4 5 6 7 8 9 10 11 12 13 14

chain bonds:

4-27 6-22 7-13 8-21 10-16 10-19 11-17 13-20 14-15 14-26 17-18 27-28 28-29 28-30 30-31 30-32

ring bonds:

1-2 1-6 2-3 2-7 3-4 3-9 4-5 5-6 7-8 8-9 10-11 10-14 11-12 12-13 13-14

exact/norm bonds:

2-7 3-9 4-27 7-8 7-13 8-9 10-11 10-14 10-16 11-12 12-13 13-14 14-15 27-28 28-30 30-31 30-32

exact bonds:

6-22 8-21 10-19 11-17 13-20 14-26 17-18 28-29

normalized bonds:

1-2 1-6 2-3 3-4 4-5 5-6

G1:CH3,NH2,H

G2:CH3,OH,MeO

G3:CN

Match level:

Search For independent claims 6+7 where

2 = CH3 + X 15!

20-N-0-0 K

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:CLAS\$16:CLAS\$17:CLAS\$18:CLAS\$19:CLAS\$20:CLAS\$21:CLAS\$22:CLAS\$ 26:CLAS\$27:CLAS\$29:CLAS\$30:CLAS\$31:CLAS\$32:CLAS\$

Welcome to STN International! Enter x:x

LOGINID:ssspta1600txm

PASSWORD:

* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * * * SESSION RESUMED IN FILE 'REGISTRY' AT 15:30:31 ON 06 JUL 2006 FILE 'REGISTRY' ENTERED AT 15:30:31 ON 06 JUL 2006 COPYRIGHT (C) 2006 American Chemical Society (ACS)

COST IN U.S. DOLLARS

SINCE FILE TOTAL
ENTRY SESSION
167.38 1496.27

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE TOTAL

CA SUBSCRIBER PRICE

DISCOUNT AMOUNTS (FOR QUALIFFING ACCOUNTS)

ENTRY SESSION

-16.50

CA SUBSCRIBER PRICE

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L35 STRUCTURE UPLOADED

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L35 HAS NO ANSWERS

L35

STR

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED - 5 TO ITERATE

100.0% PROCESSED 5 ITERATIONS 0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**

PROJECTED ITERATIONS: 5 TO 234
PROJECTED ANSWERS: 0 TO 0

L36 0 SEA SSS SAM L35

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FULL SCREEN SEARCH COMPLETED - 106 TO ITERATE

100.0% PROCESSED 106 ITERATIONS 2 ANSWERS SEARCH TIME: 00.00.01

L37 2 SEA SSS FUL L35

=> d 1-2 137

L37 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2006 ACS on STN RN 565435-21-4 REGISTRY

ED Entered STN: 13 Aug 2003

CN Carbamic acid, [[9-(2-C-methyl-β-D-ribofuranosyl)-9H-purin-6-yl]oxy], phenylmethyl ester (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C19 H21 N5 O7

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L37 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2006 ACS on STN

RN 565435-20-3 REGISTRY

ED Entered STN: 13 Aug 2003

CN Carbamic acid, [[9-(2-C-methyl- β -D-ribofuranosyl)-9H-purin-6-yl]oxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C16 H23 N5 O7

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

- 1 REFERENCES IN FILE CA (1907 TO DATE)
- 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST

338.56 1667.45

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE TOTAL ENTRY SESSION

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FILE COVERS 1907 - 6 Jul 2006 VOL 145 ISS 2 FILE LAST UPDATED: 5 Jul 2006 (20060705/ED)

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=> s 135

REG1stRY INITIATED

Substance data SEARCH and crossover from CAS REGISTRY in progress... Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

SAMPLE SEARCH INITIATED 15:31:32 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 5 TO ITERATE

100.0% PROCESSED 5 ITERATIONS 0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 5 TO 234
PROJECTED ANSWERS: 0 TO 0

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L39 0 L38

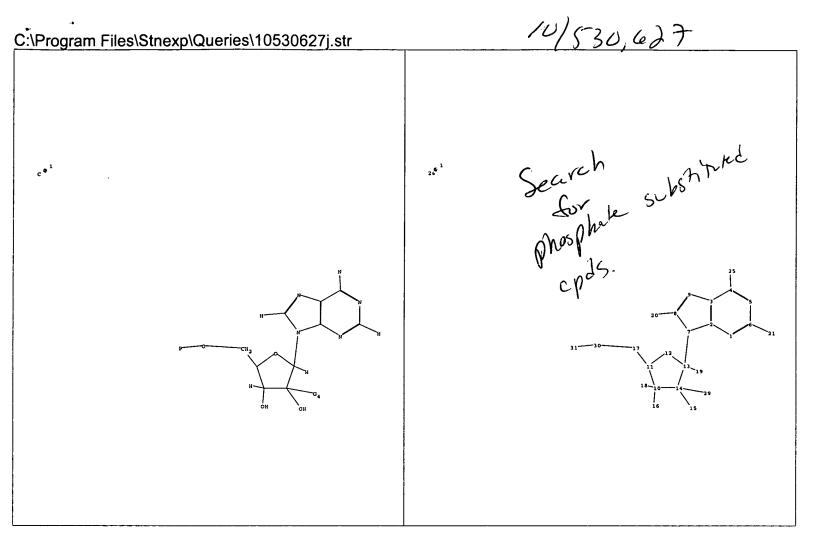
=> s 137

L40 1 L37

=> d bib 140

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ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN
L40
AN
     2003:591196 CAPLUS
DN
     139:133790
TI
     Preparation of 2'-β-modified-6-substituted adenosine analogs and
     their use as antiviral agents
IN
     An, Haoyun; Ding, Yili; Shaw, Stephanie; Hong, Zhi
PA
     Ribapharm Inc., USA
     PCT Int. Appl., 45 pp.
so
     CODEN: PIXXD2
DT
     Patent
     English
LA
FAN.CNT 4
     PATENT NO.
                       KIND
                               DATE
                                        APPLICATION NO.
     ______
                        ____
                               -----
                                          -----
ΡI
     WO 2003062256
                        A1
                               20030731 WO 2002-US34026
                                                                 20021023
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            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
            PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
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            FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
            CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI US 2002-350296P
                        Ρ
                               20020117
    MARPAT 139:133790
RE.CNT 4
             THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
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ALL CITATIONS AVAILABLE IN THE RE FORMAT



chain nodes:

15 16 17 18 19 20 21 25 29 30 31

ring nodes:

1 2 3 4 5 6 7 8 9 10 11 12 13 14

ring/chain nodes:

26

chain bonds:

4-25 6-21 7-13 8-20 10-16 10-18 11-17 13-19 14-15 14-29 17-30 30-31

ring bonds:

1-2 1-6 2-3 2-7 3-4 3-9 4-5 5-6 7-8 8-9 10-11 10-14 11-12 12-13 13-14

exact/norm bonds:

2-7 3-9 4-25 7-8 7-13 8-9 10-11 10-14 10-16 11-12 12-13 13-14 14-15 14-29 30-31 exact bonds :

6-21 8-20 10-18 11-17 13-19 17-30

normalized bonds:

1-2 1-6 2-3 3-4 4-5 5-6

G1:CH3,NH2,H

G2:CH3,OH,MeO

G3:CN

G4:0,[*1]

Match level:

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:CLAS\$16:CLAS\$17:CLAS\$18:CLAS\$19:CLAS\$20:CLAS\$21:CLAS\$25:CLAS\$ 26:CLAS\$29:CLAS\$31:CLAS\$

FULL ESTIMATED COST

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ENTRY

0.21

SESSION

0.21

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STRUCTURE FILE UPDATES: 5 JUL 2006 HIGHEST RN 890705-10-9 DICTIONARY FILE UPDATES: 5 JUL 2006 HIGHEST RN 890705-10-9

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=>

Uploading C:\Program Files\Stnexp\Queries\10530627j.str

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.

=> s l1 sss sam

SAMPLE SEARCH INITIATED 17:39:02 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 30 TO ITERATE

100.0% PROCESSED 30 ITERATIONS 1 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 272 TO 928
PROJECTED ANSWERS: 1 TO 80

L2 1 SEA SSS SAM L1

=> d 12

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN

RN 867258-93-3 REGISTRY

ED Entered STN: 11 Nov 2005

CN Adenosine 5'-(trihydrogen diphosphate), 2'-C-methyl-, $P' \rightarrow 5'$ -ester with 2-[2,3-O-(1-methylethylidene)- β -D-ribofuranosyl]-4-thiazolecarboxamide, diammonium salt (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C23 H31 N7 O14 P2 S . 2 H3 N

SR CA

LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER CRN (849146-59-4)

Absolute stereochemistry.

PAGE 1-A

PAGE 2-A

●2 NH3

- 1 REFERENCES IN FILE CA (1907 TO DATE)
- 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s l1 sss full FULL SEARCH INITIATED 17:39:22 FILE 'REGISTRY' FULL SCREEN SEARCH COMPLETED - 439 TO ITERATE

100.0% PROCESSED 439 ITERATIONS

18 ANSWERS

SEARCH TIME: 00.00.01

L3 18 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST 168.84 169.05

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=> s 13

L4 16 L3

=> d bib abs hitstr 1-16 l3 YOU HAVE REQUESTED DATA FROM FILE 'REGISTRY' - CONTINUE? (Y)/N:n

=> d bib abs hitstr 1-16 14

- L4 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
- AN 2006:136728 CAPLUS
- DN 144:324202
- TI The Novel Nucleoside Analog R1479 (4'-Azidocytidine) Is a Potent Inhibitor of NS5B-dependent RNA Synthesis and Hepatitis C Virus Replication in Cell Culture
- AU Klumpp, Klaus; Leveque, Vincent; Le Pogam, Sophie; Ma, Han; Jiang, Wen-Rong; Kang, Hyunsoon; Granycome, Caroline; Singer, Margaret; Laxton, Carl; Hang, Julie Qi; Sarma, Keshab; Smith, David B.; Heindl, Dieter; Hobbs, Chris J.; Merrett, John H.; Symons, Julian; Cammack, Nick; Martin, Joseph A.; Devos, Rene; Najera, Isabel
- CS Roche Palo Alto LLC, Palo Alto, CA, 94304, USA
- SO Journal of Biological Chemistry (2006), 281(7), 3793-3799 CODEN: JBCHA3; ISSN: 0021-9258
- PB American Society for Biochemistry and Molecular Biology
- DT Journal
- LA English
- AB Hepatitis C virus (HCV) polymerase activity is essential for HCV replication. Targeted screening of nucleoside analogs identified R1479 (4'-azidocytidine) as a specific inhibitor of HCV replication in the HCV subgenomic replicon system (IC50 = 1.28 µM) with similar potency compared with 2'-C-methylcytidine (IC50 = 1.13 μM). R1479 showed no effect on cell viability or proliferation of HCV replicon or Huh-7 cells at concns. up to 2 mM. HCV replicon RNA could be fully cleared from replicon cells after prolonged incubation with R1479. The corresponding 5'-triphosphate derivative (R1479-TP) is a potent inhibitor of native HCV replicase isolated from replicon cells and of recombinant HCV polymerase (NS5B) -mediated RNA synthesis activity. R1479-TP inhibited RNA synthesis as a CTP-competitive inhibitor with a Ki of 40 nM. On an HCV RNA-derived template substrate (complementary internal ribosome entry site), R1479-TP showed similar potency of NS5B inhibition compared with 3'-dCTP. R1479-TP was incorporated into nascent RNA by HCV polymerase and reduced further elongation with similar efficiency compared with 3'-dCTP under the reaction conditions. The S282T point mutation in the coding sequence of NS5B confers resistance to inhibition by 2'-C-MeATP and other 2'-methyl-nucleotides. In contrast, the S282T mutation did not confer cross-resistance to R1479.
- IT 374750-27-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(novel nucleoside analog R1479 (4'-azidocytidine) is a potent inhibitor of NS5B-dependent RNA synthesis and hepatitis C virus replication in cell culture)

RN 374750-27-3 CAPLUS

CN Adenosine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$NH_2$$
 NH_2
 NH_2

RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2006:100316 CAPLUS

DN 144:192451

TI Preparation of nucleoside aryl phosphoramidates for use as an inhibitor of hepatitis C virus NS5B polymerase, RNA-dependent RNA polymerase, RNA viral replication and treating RNA-dependent RNA viral infections

IN Maccoss, Malcolm; Olsen, David B.

PA Merck & Co., Inc., USA

SO PCT Int. Appl., 40 pp. CODEN: PIXXD2

DT Patent

LA English

DAN CUM 1

FAN.CNT 1																			
	PATENT NO.					KIND		DATE		APPLICATION NO.						DATE			
							-									-			
ΡI	WO 2006012078			A2 20060202			Ţ	WO 2	005-1		20050620								
	WO	2006	0120	78		A3		20060601											
		W:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	AZ,	BA,	BB,	BG,	BR,	BW,	BY,	ΒZ,	CA,	CH,	
			CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,	
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			SL,	SM,	SY,	ΤJ,	TM,	TN,	TR,	TT,	TZ,	UA,	ŪĠ,	US,	UΖ,	VC,	VN,	YU,	
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			KZ,	MD,	RU,	TJ,	TM												
PRAI	US	2004	-582	667P		P		2004	0624										
	US 2004-619746P					P		2004	1018										
os	MARPAT 144:192451																		
GT																			

AB Nucleoside aryl phosphoramidates I, wherein Y is (un)substituted C or N; Ar is (un)substituted Ph; R1 is hydrogen, fluoro, azido, amino, hydroxy, C1-3 alkoxy, mercapto, and C1-3 alkylthio; R2 and R3 are each independently selected from the group consisting of hydrogen, Me, C1-16 alkylcarbonyl, C2-18 alkenylcarbonyl, C1-10 alkyloxycarbonyl, C3-6 cycloalkylcarbonyl, and C3-6 cycloalkyloxycarbonyl; R4 is hydrogen, halogen, Me, azido, or amino; R5 and R6 are each independently selected from the group consisting of hydrogen, hydroxy, halogen, C1-4 alkoxy, amino, C1-4 alkylamino, di (C1-4 alkyl) amino, C3-6 cycloalkylamino, di (C3-6 cycloalkyl)amino, benzylamino, dibenzylamino, or C4-6 heterocycloalkyl, wherein alkyl, cycloalkyl, benzyl, and heterocycloalkyl; R7 is hydrogen, C1-5 alkyl, (un)substituted Ph or benzyl; R8 is hydrogen, C1-6 alkyl, C3-6 cycloalkyl, (un)substituted Ph or benzyl; R9 is hydrogen or Me, were prepared as precursors to inhibitors of RNA-dependent RNA viral polymerase. Nucleoside anyl phosphoramidates, I, alone or in combination with other agents active against RNA-dependent RNA polymerase, inhibiting RNA-dependent RNA viral replication, and/or treating RNA-dependent RNA viral infection. Thus, II was prepared (no yield) and tested as an inhibitor of hepatitis C virus (HCV) NS5B polymerase, as precursors to inhibitors of HCV replication, and/or for the treatment of hepatitis C infection (EC50 less than 100 μM).

Ι

IT 874883-59-7P 874883-60-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of nucleoside aryl phosphoramidates for use as an inhibitors of hepatitis C virus NS5B polymerase, RNA-dependent RNA polymerase, RNA viral replication and treating RNA-dependent RNA viral infections)

RN 874883-59-7 CAPLUS

CN L-Alanine, N-[[P(S)]-2'-C-methyl-P-phenyl-5'-adenylyl]-, methyl ester
(9CI) (CA INDEX NAME)

CN L-Alanine, N-[[P(R)]-2'-C-methyl-P-phenyl-5'-adenylyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2005:410482 CAPLUS

DN 143:444

TI Inhibitory effect of 2'-substituted nucleosides on hepatitis C virus replication correlates with metabolic properties in replicon cells

AU Tomassini, Joanne E.; Getty, Krista; Stahlhut, Mark W.; Shim, Sung; Bhat, Balkrishen; Eldrup, Anne B.; Prakash, Thazha P.; Carroll, Steven S.; Flores, Osvaldo; MacCoss, Malcolm; McMasters, Daniel R.; Migliaccio, Giovanni; Olsen, David B.

CS Department of Antiviral Research, Merck Research Laboratories, West Point, PA, 19486, USA

SO Antimicrobial Agents and Chemotherapy (2005), 49(5), 2050-2058 CODEN: AMACCQ; ISSN: 0066-4804

PB American Society for Microbiology

DT Journal

LA English

RN

AB Nucleosides have been widely used in the treatment of viral diseases, but relatively few have been identified as inhibitors of hepatitis C virus (HCV). The modified ribonucleosides, 2'-C-methyl-adenosine and 2'-O-methyl-cytidine, are potent inhibitors of HCV replication which specifically target the NS5B polymerase. Herein, a more extensive characterization of the effect of these compds. upon HCV replication in subgenomic replicons is reported. A highly selective antireplicative effect induced by the nucleosides in replicon-containing cell lines was maintained during an exponential growth period with potencies which paralleled the reduction of both pos.- and neg.-strand RNA replication. Moreover, the inhibitory effect closely correlated with the intrinsic metabolic properties of differing replicon clonal lines. Interestingly, while 2'-C-methyl-adenosine elicited similar inhibitory potencies in different cell lines, 2'-O-methyl-cytidine was found to be inactive in one replicon cell line tested, although the corresponding triphosphates comparably inhibited the in vitro activity of replication complexes isolated from these cells and the activity of NS5B polymerase using synthetic templates. The lack of antireplicative effect, attributed to poor intracellular conversion of the 2'-O-methyl-cytidine nucleoside to the active 5'-triphosphate, was reversed using a monophosphate prodrug. Thus, although replicon cells are useful for evaluating the effect of inhibitors upon HCV replication, these findings have important implications for their use in the identification and characterization of nucleosides and other chemotherapeutic agents requiring cellular metabolism IT 374750-27-3

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitory effect of 2'-substituted nucleosides on hepatitis C virus replication correlates with metabolic properties in replicon cells) 374750-27-3 CAPLUS

CN Adenosine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L4 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
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AN 2005:216597 CAPLUS

DN 142:291323

TI Compositions and methods for the treatment of severe acute respiratory syndrome (SARS)

0

IN Hardee, Greg; Dellamary, Luis

PA Isis Pharmaceuticals, Inc., USA

SO PCT Int. Appl., 217 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.					KIND DATE				APPL	ICAT		DATE				
PI		05020885 05020885		A2 20050310 A3 20050804		WO 2004-US16196						20040521					
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			TD,		Br,	, טם	Cr,	CG,	CI,	CI-1,	GA,	GIV,	GQ,	GW,	иш,	PIRC,	NE,

PRAI US 2003-472774P P 20030521

AB The invention provides compns. and methods for treating a coronavirus infection, especially a SARS CoV infection. The compns. comprise an antiviral nucleoside or mimetic thereof, or an antiviral antisense agent, in a form suitable for pulmonary or nasal delivery. The methods comprise administration to a patient in need thereof the effective amount of an antiviral composition by pulmonary or nasal instillation.

IT 374750-27-3 444019-70-9 847651-45-0

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(compns. and methods for treatment of severe acute respiratory syndrome)

RN 374750-27-3 CAPLUS

CN Adenosine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 444019-70-9 CAPLUS
CN 5'-Adenylic acid, 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 847651-45-0 CAPLUS

CN 9H-Purin-6-amine, 9-[5-0-[hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-2-C-methyl-β-D-arabinofuranosyl]- (9CI) (CA INDEX NAME)

- L4 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
- AN 2005:150037 CAPLUS
- DN 142:348134
- TI Synthesis, conformational analysis, and biological activity of new analogues of thiazole-4-carboxamide adenine dinucleotide (TAD) as IMP dehydrogenase inhibitors
- AU Franchetti, Palmarisa; Cappellacci, Loredana; Pasqualini, Michela; Petrelli, Riccardo; Jayaprakasan, Vetrichelvan; Jayaram, Hiremagalur N.; Boyd, Donald B.; Jain, Manojkumar D.; Grifantini, Mario
- CS Dipartimento di Scienze Chimiche, Universita di Camerino, Camerino, 62032, Italy

SO Bioorganic & Medicinal Chemistry (2005), 13(6), 2045-2053 CODEN: BMECEP; ISSN: 0968-0896

PB Elsevier Ltd.

DT Journal

LA English

OS CASREACT 142:348134

AB Thiazole-4-carboxamide adenine dinucleotide (TAD) analogs T-2'-MeAD (1) and T-3'-MeAD (2) containing, resp., a Me group at the ribose 2'-C-, and 3'-C-position of the adenosine moiety, were prepared as potential selective human inosine monophosphate dehydrogenase (IMPDH) type II inhibitors. The synthesis of heterodinucleotides was carried out by CDI-catalyzed coupling reaction of unprotected 2'-C-methyl- or 3'-C-methyl-AMP with 2',3'-O-isopropylidene-tiazofurin 5'-monophosphate, and then deisopropylidenation. Biol. evaluation of dinucleotides 1 and 2 as inhibitors of recombinant human IMPDH type I and type II resulted in a Inhibition of both isoenzymes by T-2'-MeAD and T-3'-MeAD good activity. was noncompetitive with respect to NAD substrate. Binding of T-3'-MeAD was comparable to that of parent compound TAD, while T-2'-MeAD proved to be a weaker inhibitor. However, no significant difference was found in inhibition of the IMPDH isoenzymes. T-2'-MeAD and T-3'-MeAD were found to inhibit the growth of K562 cells (IC50 30.7 and 65.0 μM, resp.).

IT 867258-82-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis, conformational anal., and biol. activity of new analogs of thiazole-4-carboxamide adenine dinucleotide (TAD) as IMP dehydrogenase inhibitors)

RN 867258-82-0 CAPLUS

Absolute stereochemistry.

●2 NH3

PAGE 1-B

-NH₂

IT 444019-70-9P 849146-56-1P 849146-61-8P 867258-93-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis, conformational anal., and biol. activity of new analogs of thiazole-4-carboxamide adenine dinucleotide (TAD) as IMP dehydrogenase inhibitors)

RN 444019-70-9 CAPLUS

CN 5'-Adenylic acid, 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 849146-56-1 CAPLUS

CN Adenosine, 2'-C-methyl-, 5'-(hydrogen 1H-imidazol-1-ylphosphonate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 849146-61-8 CAPLUS

CN Adenosine 5'-(trihydrogen diphosphate), 2'-C-methyl-, $P' \rightarrow 5'$ -ester with 2'-C-methyladenosine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

RN 867258-93-3 CAPLUS

CN Adenosine 5'-(trihydrogen diphosphate), 2'-C-methyl-, P' \rightarrow 5'-ester with 2-[2,3-O-(1-methylethylidene)- β -D-ribofuranosyl]-4-thiazolecarboxamide, diammonium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 2-A

●2 NH3

RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L4 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
- AN 2005:34765 CAPLUS
- DN 142:94074
- TI Preparation of modified fluorinated (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl nucleoside analogs as antiviral agents
- IN Clark, Jeremy
- PA Pharmasset, Ltd., Barbados
- SO PCT Int. Appl., 228 pp. CODEN: PIXXD2
- DT Patent
- LA English

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FAN.CNT 1
     PATENT NO.
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                                DATE
                                           APPLICATION NO.
                                                                   DATE
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     WO 2005003147
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     WO 2005003147
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                                20050303
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PRAI US 2003-474368P
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     WO 2004-US12472
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OS
     MARPAT 142:94074
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$$R^{1}O$$
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Ι

GI

AB The disclosed invention provides nucleoside analogs I, wherein B is purine and pyrimidine nucleobase; X is O, S, CH2, Se, NH, N-alkyl, CHW, C(W)2; W is F, Cl, Br, iodo; R1 is H, phosphate, H-phosphonate, acyl, Ph, alkyl, carboxyalkylamino, sulfonate ester, peptide, amino acid, sugar reside; R2 and R2' are independently H, alkyl, alkenyl, alkynyl, vunyl, N3, CN, halogen, NO2, ester, alkoxy, thioalkyl, sulfoxide, sulfonyl; R6 is alkyl, CN, Me, OMe, OEt, CH2OH, CH2F, N3, CHCN, CH2N3, CH2NH2, CH2NHMe, CH2NMe2, alkylne; and methods of treating a Flaviviridae infection, including hepatitis C virus, West Nile Virus, yellow fever virus, and a rhinovirus infection in a host, including animals, and especially human, using a (2'R)-2'-deoxy-2'-fluoro-2'-C-Me nucleosides, or a pharmaceutically acceptable salt or prodrug thereof. Thus, (2'R)-2'-deoxy-2'-fluoro-2'-Cmethylcytidine was prepared and tested as antiviral agent. The effects the nucleoside analogs tested on human bone marrow cells are reported. (2'R)-2'-deoxy-2'-fluoro-2'-C-methylcytidine shows activity against Rhinovirus, West Nile virus, Yellow Fever virus, and Dengue virus. Cytotoxicity and effect of nucleoside analogs on human bone marrow cells are reported. IT 374750-27-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
 (preparation of modified fluorinated (2'R)-2'-deoxy-2'-fluoro-2'-C-Me
 nucleoside analogs as antiviral agents)

RN 374750-27-3 CAPLUS

CN Adenosine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:1127101 CAPLUS

DN 142:49201

TI Inhibiting Coronaviridae viral replication and treating Coronaviridae viral infection with nucleoside compounds

IN Olsen, David B.; Tomassini, Joanne E.; Mao, Shi-Shan; Carroll, Steven S.

PA USA

SO U.S. Pat. Appl. Publ., 19 pp., which

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE		
ΡI	US 2004259934	A1	20041223	US 2004-832945	20040427		
PRAI	US 2003-467068P	P	20030501				
	US 2003-470658P	P	20030515				

OS MARPAT 142:49201

AB Infection by a Coronaviridae virus (e.g. a coronavirus) and/or illness due to a Coronaviridae virus are treated or protected against by administration of a therapeutically or prophylactically effective amount of certain nucleoside compds. and derivs. thereof, either alone or in a composition comprising the nucleoside compound or its derivative and a pharmaceutically acceptable carrier. In addition, replication of a Coronaviridae virus is inhibited by administration of the nucleoside compds. and derivs. thereof, either alone or in pharmaceutical compns. The nucleosides are particularly suitable for use in treating or prophylaxis of an infection by the SARS virus and/or in treating or prophylaxis of SARS, and for use in inhibiting replication of the SARS virus. The nucleoside compds. and derivs. can optionally be administered in combination with other agents active against the Coronaviridae virus and/or an illness due to the virus. The nucleoside compds. are also for use in the manufacture of medicaments for the inhibition of Coronaviridae virus replication, for the treatment or prophylaxis of Coronaviridae virus infection, and/or for the treatment or prophylaxis of an illness due to a Coronaviridae virus (e.g., the SARS virus). In addition, the compds. are for use as medicaments for the inhibition of Coronaviridae virus replication, for the treatment or prophylaxis of Coronaviridae virus infection, and/or for the treatment or prophylaxis of an illness due to a Coronaviridae virus. Compds. of the invention include e.g. 4-Amino-7-(2-C-methyl- β -D-ribofuranosyl) -7H-pyrrolo[2,3-d]pyrimidine (preparation described). IT 374750-27-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(nucleoside compds. for inhibition of Coronaviridae viral replication and treating Coronaviridae viral infection)

RN 374750-27-3 CAPLUS

CN Adenosine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4ANSWER 8 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:848340 CAPLUS

DN 142:226

A 7-deaza-adenosine analog is a potent and selective inhibitor of TIhepatitis C virus replication with excellent pharmacokinetic properties ΑU Olsen, David B.; Eldrup, Anne B.; Bartholomew, Linda; Bhat, Balkrishen; Bosserman, Michele R.; Ceccacci, Alessandra; Colwell, Lawrence F.; Fay, John F.; Flores, Osvaldo A.; Getty, Krista L.; Grobler, Jay A.; LaFemina, Robert L.; Markel, Eric J.; Migliaccio, Giovanni; Prhavc, Marija; Stahlhut, Mark W.; Tomassini, Joanne E.; MacCoss, Malcolm; Hazuda, Daria J.; Carroll, Steven S.

CS Department of Biological Chemistry, Merck Research Laboratories, West Point, PA, USA

SO Antimicrobial Agents and Chemotherapy (2004), 48(10), 3944-3953 CODEN: AMACCQ; ISSN: 0066-4804

PB American Society for Microbiology

DT Journal

LA English

AB Improved treatments for chronic hepatitis C virus (HCV) infection are needed due to the suboptimal response rates and deleterious side effects associated with current treatment options. The triphosphates of 2'-C-methyl-adenosine and 2'-C-methyl-guanosine were previously shown to be potent inhibitors of the HCV RNA-dependent RNA polymerase (RdRp) that is responsible for the replication of viral RNA in cells. Here we demonstrate that the inclusion of a 7-deaza modification in a series of purine nucleoside triphosphates results in an increase in inhibitory potency against the HCV RdRp and improved pharmacokinetic properties. Notably, incorporation of the 7-deaza modification into 2'-C-methyl-adenosine results in an inhibitor with a 20-fold-increased potency as the 5'-triphosphate in HCV RdRp assays while maintaining the inhibitory potency of the nucleoside in the bicistronic HCV replicon and with reduced cellular toxicity. In contrast, while 7-deaza-2'-C-methyl-GTP also displays enhanced inhibitory potency in enzyme assays, due to poor cellular penetration and/or metabolism, the nucleoside does not inhibit replication of a bicistronic HCV replicon in cell culture. 7-Deaza-2'-C-methyl-adenosine displays promising in vivo pharmacokinetics in three animal species, as well as an acute oral LD in excess of 2,000 mg/kg of body weight in mice. Taken together, these data demonstrate that 7-deaza-2'-C-methyl-adenosine is an attractive candidate for further investigation as a potential treatment for HCV infection. IT 374750-27-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(a 7-deaza-adenosine analog is a potent and selective inhibitor of hepatitis C virus replication with excellent pharmacokinetic

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properties)
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RN 374750-27-3 CAPLUS

CN Adenosine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:290484 CAPLUS

DN 140:327061

TI Nucleoside derivatives for treating hepatitis C virus infection

IN Roberts, Christopher Don; Dyatkina, Natalia B.

PA Genelabs Technologies, Inc., USA

SO PCT Int. Appl., 119 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN. CNT 2

FAN.	PATENT NO.						KIND DATE				ΔΡΡΙ,	TCAT		DATE				
ΡI	WO				A2 20040408			WO 2003-US31433						20030930				
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			GM,	HR,	HU,	ID,	ID, IL, IN, IS,				KE,	KG,	ΚP,	KR,	ΚZ,	LC,	LK,	LR,
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			TR,	TT,	TZ,	UA,	ŪĠ,	US,	UΖ,	VC,	VN,	ΥU,	ZA,	ZM,	zw			
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	ΑU	2003	2797	97		A1 20040419			AU 2003-279797									
	EP	1572	097			A2 20050914					EP 2	003-		20030930				
	ΕP	1572	097			A3 20051207												
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	NO	0 2005001969			Α		2005	0524	NO 2005-1969									
PRAI			2002-415222P					2002										
		2003																
	WO	2003	-US3	1433		W		2003	0930									
os	MARPAT 140:327061																	

AB Nucleoside compns. and methods for treating hepatitis C virus infections. Thus, 9-(2'-C-methyl- β -D-ribofuranosyl)-6-methoxyaminopurine was prepared by the reaction of 6-chloro-9-(2'-C-methyl- β -D-ribofuranosyl)purine and methxylamine. This compound exhibited anti-hepatitis C activity by inhibiting HCV polymerase.

(CA

Absolute stereochemistry.

INDEX NAME)

L4 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:2898 CAPLUS

DN 140:42424

TI Preparation of nucleoside derivatives as inhibitors of RNA-dependent RNA viral polymerase

IN Carroll, Steven S.; Olsen, David B.; Durette, Philippe L.; Bhat, Balkrishen; Dande, Prasad; Eldrup, Anne B.

PA Merck & Co., Inc., USA; Isis Pharmaceuticals, Inc.

SO PCT Int. Appl., 43 pp. CODEN: PIXXD2

CODEN: PI

DT Patent

LA English FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ----------------------------------PΙ WO 2004000858 A2 20031231 WO 2003-US19172 20030617 WO 2004000858 Α3 20050512 AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, W: CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG CA 2488534 AA 20031231 CA 2003-2488534 20030617 AU 2003269890 20040106 AU 2003-269890 Α1 20030617 EP 1551421 A2 20050713 EP 2003-751777 20030617 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK JP 2005530843 T2 20051013 JP 2004-515870 20030617 PRAI US 2002-390579P Р 20020621 WO 2003-US19172 W 20030617 os MARPAT 140:42424 GI

AB The present invention provides nucleoside compds. I, wherein B is nucleobase; R1 is fluoromethyl, difluoromethyl, trifluoromethyl; R2 is H, F, amino, OH, SH, alkoxy, alkylcarbonyloxy, alkyl; R3 and R4 are independently H, Cn, N3, halogen, OH, SH, amino, alkoxy, alkylcarconyloxy, alkenyl, alkynyl; R5 is H, alkylcarbonyl, P3O9H4, P2O6H3, phosphophonyl; R6 and R7 independently H, Me, hydroxymethyl, fluoromethyl; and certain derivs. thereof which are inhibitors of RNA-dependent RNA viral polymerase. These compds. are inhibitors of RNA-dependent RNA viral replication and are useful for the treatment of RNA-dependent RNA viral infection. They are particularly useful as inhibitors of hepatitis C virus (HCV) NS5B polymerase, as inhibitors of HCV replication, and/or for the treatment of hepatitis C infection. The invention also describes pharmaceutical compns. containing such nucleoside compds. alone or in combination with other agents active against RNA-dependent RNA viral infection, in particular HCV infection. Also disclosed are methods of inhibiting RNA-dependent RNA polymerase, inhibiting RNA-dependent RNA viral replication, and/or treating RNA-dependent RNA viral infection with the nucleoside compds. of the present invention. Thus, 2-amino-9-(2-C-fluoromethyl- β -D-ribofuranosyl)-3,9-dihydropurin-6-one was prepared and tested as inhibitor of RNA-dependent RNA viral polymerase. Title compds. tested in the HCV NS5B polymerase assay exhibited IC50's less than 100 µmol.

IT 636581-94-7P 636581-95-8P 636582-00-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of nucleoside derivs. as inhibitors of RNA-dependent RNA viral polymerase)

RN 636581-94-7 CAPLUS

CN Adenosine 5'-(tetrahydrogen triphosphate), 2'-C-(fluoromethyl)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

RN 636581-95-8 CAPLUS

CN 9H-Purin-6-amine, 9-[2-C-(fluoromethyl)-5-0-[hydroxy[[hydroxy(phosphonooxy

)phosphinyl]oxy]phosphinyl]- β -D-arabinofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 636582-00-8 CAPLUS

CN Adenosine 5'-(tetrahydrogen triphosphate), 2'-C-(fluoromethyl)-N-methyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2003:247410 CAPLUS

DN 139:111121

TI Inhibition of Hepatitis C Virus RNA Replication by 2'-Modified Nucleoside Analogs

AU Carroll, Steven S.; Tomassini, Joanne E.; Bosserman, Michele; Getty, Krista; Stahlhut, Mark W.; Eldrup, Anne B.; Bhat, Balkrishen; Hall, Dawn; Simcoe, Amy L.; LaFemina, Robert; Rutkowski, Carrie A.; Wolanski, Bohdan; Yang, Zhucheng; Migliaccio, Giovanni; De Francesco, Raffaele; Kuo, Lawrence C.; MacCoss, Malcolm; Olsen, David B.

CS Department of Biological Chemistry, Merck Research Laboratories, West Point, PA, 19486, USA

SO Journal of Biological Chemistry (2003), 278(14), 11979-11984 CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

AB The RNA-dependent RNA polymerase (NS5B) of hepatitis C virus (HCV) is essential for the replication of viral RNA and thus constitutes a valid target for the chemotherapeutic intervention of HCV infection. In this report, we describe the identification of 2'-substituted nucleosides as inhibitors of HCV replication. The 5'-triphosphates of 2'-C-methyladenosine and 2'-O-methylcytidine are found to inhibit NS5B-catalyzed RNA synthesis in vitro, in a manner that is competitive with substrate nucleoside triphosphate. NS5B is able to incorporate

either nucleotide analog into RNA as determined with gel-based incorporation assays but is impaired in its ability to extend the incorporated analog by addition of the next nucleotide. In a subgenomic replicon cell line, 2-C-methyladenosine and 2'-O-methylcytidine inhibit HCV RNA replication. The 5'-triphosphates of both nucleosides are detected intracellularly following addition of the nucleosides to the media. However, significantly higher concns. of 2'-C-methyladenosine triphosphate than 2'-O-methylcytidine triphosphate are detected, consistent with the greater potency of 2'-C-methyladenosine in the replicon assay, despite similar inhibition of NS5B by the triphosphates in the in vitro enzyme assays. Thus, the 2'-modifications of natural substrate nucleosides transform these mols. into potent inhibitors of HCV replication.

IT 374750-27-3

> RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(inhibition of hepatitis C virus RNA replication by 2'-modified nucleoside analogs)

RN 374750-27-3 CAPLUS

CN Adenosine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (9CI) (CA INDEX

Absolute stereochemistry.

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2002:555629 CAPLUS

DN 137:125359

TI Preparation of nucleoside derivatives as inhibitors of RNA-dependent RNA viral polymerase

IN Carroll, Steven S.; Lafemina, Robert L.; Hall, Dawn L.; Himmelberger, Amy L.; Kuo, Lawrence C.; Maccoss, Malcolm; Olsen, David B.; Rutkowski, Carrie A.; Tomassini, Joanne E.; An, Haoyun; Bhat, Balkrishen; Bhat, Neelima; Cook, Phillip Dan; Eldrup, Anne B.; Guinosso, Charles J.; Prhavc, Marija; Prakash, Thazha P.

PA Merck & Co., Inc., USA; Isis Pharmaceuticals, Inc.

SO PCT Int. Appl., 235 pp. CODEN: PIXXD2

DT Patent

English LA

FAN.	CNT 2															
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ΡI	WO 2002	057425		A2	2002	0725	1	WO 2	002-1	US15	31		20	0020	118	
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PRAI US 2001-263313P
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     US 2002-52318
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                                 20020118
     WO 2002-US1531
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     US 2003-431657
                                 20030507
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     MARPAT 137:125359
GΙ
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AB The present invention provides the preparation of nucleoside compds. I, wherein B is nucleobase, Y is H, alkylcarbonyl, phosphate; R1 is H, alkenyl, alkynyl, alkyl; R2 and R3 are independently H, OH, halogen, alkyl, alkoxy, alkenyloxy, alkylthio, alkylcarbonyloxy, aryloxycrbonyl, azido, amino, alkylamino; R1 and R2 together with the carbon atom to which they are attached form a 3- to 6-membered heterocycle; R4 is H, OH, SH, NH2, alkylamino, cycloalkylamino, halogen, alkyl, alkoxy, CF3; R5 and R6 are independently H, hydroxymethyl, Me, fluoromethyl; and certain derivs. thereof which are inhibitors of RNA-dependent RNA viral polymerase. compds. are inhibitors of RNA-dependent RNA viral replication and are useful for the treatment of RNA-dependent RNA viral infection. They are particularly useful as inhibitors of hepatitis C virus (HCV) NS5B polymerase, as inhibitors of HCV replication, and/or for the treatment of hepatitis C infection. The invention also describes pharmaceutical compns. containing such nucleoside compds. alone or in combination with other agents active against RNA-dependent RNA viral infection, in particular HCV infection. Also disclosed are methods of inhibiting RNA-dependent RNA polymerase, inhibiting RNA-dependent RNA viral replication, and/or treating RNA-dependent RNA viral infection with the nucleoside compds. of the present invention. Thus, $4-amino-1-(2-C-methyl-\beta-D-methyl-3-methyl$ ribofuranosyl)-1H-pyrazolo[3,4-d]pyrimidine was prepared as inhibitors of RNA-dependent RNA viral polymerase. Representative compds. tested in the HCV NS5B polymerase assay exhibited IC's less than 100 μM . The compds. of the present invention were also evaluated for their ability to affect the replication of Hepatitis C Virus RNA in cultured hepatoma (HuH-7) cells containing a sub-genomic HCV Replicon.

Absolute stereochemistry.

RN 444019-70-9 CAPLUS CN 5'-Adenylic acid, 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Absolute stereochemistry.

L4

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AN
     2001:886155 CAPLUS
DN
     136:590
     Methods and compositions using modified nucleosides for treating
ΤI
     flaviviruses and pestiviruses
IN
     Sommadossi, Jean-Pierre; Lacolla, Paolo
     Novirio Pharmaceuticals Limited, Cayman I.; Universita Degli Studi Di
PA
     Cagliari
     PCT Int. Appl., 302 pp.
SO
     CODEN: PIXXD2
DT
     Patent
     English
LA
FAN.CNT 2
     PATENT NO.
                        KIND
                                DATE
                                           APPLICATION NO.
                                                                  DATE
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PΤ
     WO 2001092282
                         A2
                                20011206
                                           WO 2001-US16687
                                                                  20010523
     WO 2001092282
                         A3
                                20020502
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
             RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
             UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                          CA 2001-2410579
     CA 2410579
                                20011206
                         AΑ
     EP 1294735
                                20030326
                                          EP 2001-952131
                         A2
                                                                  20010523
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     US_2003060400
                         A1
                                20030327
                                           US 2001-863816
                                                                  20010523
     US 6812219
                         B2
                                20041102
     BR 2001011196
                         Α
                                20040406
                                           BR 2001-11196
                                                                  20010523
     JP 2004510698
                         T2
                                20040408
                                           JP 2002-500895
                                                                  20010523
     NO 2002005600
                        Α
                                20030117
                                           NO 2002-5600
                                                                  20021121
     ZA 2002010112
                        Α
                               20040623
                                           ZA 2002-10112
                                                                  20021212
     US 2004063622
                        A1
                               20040401
                                           US 2003-602693
                                                                  20030620
                        A1
     US 2004097462
                               20040520
                                           US 2003-602692
                                                                  20030620
     US 2004102414
                        A1
                               20040527
                                           US 2003-602694
                                                                  20030620
PRAI US 2000-207674P
                        P
                               20000526
                         P
     US 2001-283276P
                               20010411
     US 2001-863816
                         Α3
                               20010523
     WO 2001-US16687
                               20010523
OS
     MARPAT 136:590
     A method and composition are provided for treating a host infected with
AB
     flavivirus or pestivirus, comprising administering an effective amount of a
     1', 2' or 3'-modified nucleoside or a pharmaceutically acceptable salt or
     prodrug thereof.
IT
     374750-27-3
     RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); BIOL
     (Biological study)
        (nucleoside derivs. for treating flaviviruses and pestiviruses)
RN
     374750-27-3 CAPLUS
CN
     Adenosine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (9CI) (CA INDEX
     NAME)
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Absolute stereochemistry.

Column 109-110 whorein

Ri=diphosphak, R2=H=R3, RG=CH3, X=0,

Base = admin

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L4 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
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AN 2001:868467 CAPLUS

DN 136:6296

TI Preparation of antiviral nucleosides and methods for treating hepatitis C

IN Sommadossi, Jean-Pierre; Lacolla, Paulo

PA Novirio Pharmaceuticals Limited, Cayman I.; Universita degli Studi di Cagliari

SO PCT Int. Appl., 296 pp.

CODEN: PIXXD2

WO 2001-US16671

MARPAT 136:6296

os

W

DT Patent

LA English FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE PΙ WO 2001090121 A2 20011129 WO 2001-US16671 20010523 WO 2001090121 **A**3 20020502 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG CA 2409613 20011129 CA 2001-2409613 AA 20010523 AU 2001074906 **A5** 20011203 AU 2001-74906 20010523 US 2003050229 20030313 US 2001-864078 **A1** 20010523 US 6914054 B2 20050705 EP 1292603 **A2** 20030319 EP 2001-941564 20010523 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR BR 2001-11127 BR 2001011127 20030624 Α 20010523 JP 2004533401 JP 2001-586308 T2 20041104 20010523 NZ 522863 20050729 NZ 2001-522863 Α 20010523 EP 1669364 EP 2006-75216 20060614 Α2 20010523 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, RO, CY, TR NO 2002005627 20030106 NO 2002-5627 Α 20021122 ZA 2002-10101 ZA 2002010101 20040614 Α 20021212 US 2004097461 20040520 A1 US 2003-602691 20030620 US 2004101535 **A**1 20040527 US 2003-602976 20030620 US 2005124532 A1 20050609 US 2003-602142 20030620 US 2005137161 A1 20050623 US 2003-602136 20030620 PRAI US 2000-206585P Ρ 20000523 EP 2001-941564 20010523 A3 US 2001-864078 Α1 20010523

20010523

Ι

AB A method and composition for treating a host infected with hepatitis C comprising administering an effective hepatitis C treatment amount of a described 1'-, 2'- or 3'-modified nucleosides I, wherein : R1-R3 and R are independently H, phosphate (including mono, di- or triphosphate and a stabilized phosphate prodrug); acyl; alkyl; sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the Ph group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered in vivo is capable of providing a compound wherein R1-R3 are independently H or phosphate; Y is hydrogen, bromo, chloro, fluoro, iodo, OR4, NR4R5 or SR4; X1 and X2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR4, NR4R5 or SR4; and R4 and R5 are independently hydrogen, acyl, alkyl.or a pharmaceutically acceptable salt or prodrug thereof, is provided. Thus, I (R1-R3 = X1 = X2 = H, Y = NH2) was prepared and tested in Cynomolgus monkeys as antiviral agent. Oral bioavailability in monkeys, bone human bone marrow toxicity (IC50 > 10 μM), and mitochondrial toxicity, were reported . 374750-27-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of antiviral nucleosides and methods for treating hepatitis C virus)

RN 374750-27-3 CAPLUS

CN Adenosine 5'-(tetrahydrogen triphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

$$NH_2$$
 NH_2
 NH_2

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L4
     ANSWER 15 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
AN
     1996:169523 CAPLUS
DN
     124:224779
     Mechanism-based inhibition of ribonucleoside diphosphate reductase from
ΤI
     corynebacterium nephridii by 2-C-methyladenosine diphosphate
ΑU
     McFarlan, Sara C.; Ong, Seng Poon; Hogenkamp, Harry P. C.
CS
     Department of Biochemistry, University of Minnesota, Minneapolis, MN,
     55455, USA
SO
     Biochemistry (1996), 35(14), 4485-91
     CODEN: BICHAW; ISSN: 0006-2960
PB
     American Chemical Society
DT
     Journal
LΑ
     English
     The interaction of the adenosylcobalamin-dependent ribonucleoside
AB
     diphosphate reductase of Corynebacterium nephridii with
     2'-C-methyladenosine diphosphate (2'-C-methylADP) has been investigated in
     more detail [Ong, S. P., McFarlan, S. C., & Hogenkamp, H. P. C. (1993)
     Biochem. 32, 11397-11404]. This nucleotide analog partitioned between
     normal reduction to 2'-deoxy-2'-C-methyladenosine diphosphate and
decomposition to
     adenine, 2-methylene-3(2H)-4-methylfuranone, and presumably pyrophosphate.
     Reaction of the reduced enzyme with 2'-C-methylADP caused the development
     of a chromophore at 318 nm that is characteristic of the modification of
     the enzyme by the furanone [Harris, G., Ator, M., & Stubbe, J. (1984)
     Biochem. 23, 5214-5225]. Incubation of [5'-3H2]-2'-C-methylADP with
     reduced reductase resulted in the covalent incorporation of the radiolabel
     into the protein and into aquocobalamin. A similar incubation of the
     enzyme, the labeled nucleotide analog, and dithiothreitol resulted in the
     formation of three radioactive hydrophilic compds. Mass spectroscopic
     anal. of one of these compds. showed the presence of 2-methylene-3(2H)-4-
     methylfuranone. 2'-Deoxy-2'-C-methylADP is a very effective promoter of
     the tritium exchange reaction between [5'-3H2]adenosylcobalamin and the
     solvent, confirming that the exchange reaction is an integral part of the
    overall reduction All these observations are consistent with the proposal
     that 2'-C-methylADP serves as a substrate and a mechanism-based inhibitor
    of the ribonucleotide reductase of C. nephridii, indicating that the
     enzyme is able to catalyze the conversion of the nucleotide analog to a
     2'-deoxy-2'-C-methyl-3'-ketonucleotide that can collapse to the reactive
     2-methylene-3(2H)-4-methylfuranone. Surprisingly, 2'-C-methylADP did not
     serve as either a substrate or an inhibitor of the ribonucleoside
    diphosphate reductase of Escherichia coli.
    150993-72-9
```

process); BSU (Biological study, unclassified); BIOL (Biological study);
PROC (Process)
 (mechanism-based inhibition of ribonucleoside diphosphate reductase

(mechanism-based inhibition of ribonucleoside diphosphate reductase from Corynebacterium nephridii by 2-C-methyladenosine diphosphate) 150993-72-9 CAPLUS

RL: BAC (Biological activity or effector, except adverse); BPR (Biological

CN Adenosine 5'-(trihydrogen diphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN

IT 174753-96-9P

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process) (preparation of tritiated 2-C-methyladenosine diphosphate for study of mechanism-based inhibition of ribonucleoside diphosphate reductase from Corynebacterium nephridii)

RN 174753-96-9 CAPLUS

CN Adenosine-5',5'-C-t2 5'-(trihydrogen diphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$NH_2$$
 N
 NH_2
 N
 NH_2
 NH_2

L4 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1993:620274 CAPLUS

DN 119:220274

TI 2'-C-Methyladenosine and 2'-C-methyluridine 5'-diphosphates are mechanism-based inhibitors of ribonucleoside diphosphate reductase from Corynebacterium nephridii

AU Ong, Seng Poon; McFarlan, Sara C.; Hogenkamp, Harry P. C.

CS Dep. Biochem., Univ. Minnesota, Minneapolis, MN, 55455, USA

Biochemistry (1993), 32(42), 11397-404

CODEN: BICHAW; ISSN: 0006-2960

DT Journal

SO

AB

LA English

The interaction of the adenosylcobalamin-dependent ribonucleoside diphosphate reductase of Corynebacterium nephridii with 2'-C-methyladenosine 5'-diphosphate (2'-MeADP) and 2'-C-methyluridine 5'-diphosphate (2'-MeUDP) has been investigated. The nucleotide analogs are converted to adenine and uracil, resp., suggesting that they may be mechanism-based inhibitors. In addition, both analogs generate nucleotides with properties expected for the 2'-deoxy-2'-C-methylnucleotides. The nucleoside obtained after enzymic dephosphorylation of the product formed from 2'-MeADP has been identified as 2'-deoxy-2'-C-methyladenosine by 1H NMR and mass spectroscopies. Adenine is the major product derived from 2'-MeADP, indicating that the degradation pathway predominates. During the reaction, the carbon-cobalt bond of the coenzyme is cleaved irreversibly

to yield 5'-deoxyadenosine and cob(II)alamin. 2'-MeADP is a potent competitive inhibitor of the reduction of the purine nucleotides ADP and GDP, while 2'-MeUDP competitively inhibits the reduction of the pyrimidine nucleotides UDP and CDP. 2'-MeADP is a very effective promoter of the tritium exchange reaction between [5'-3H2]adenosylcobalamin and the solvent, indicating that the exchange reaction is an integral part of the overall reduction All these observations are consistent with the reaction mechanism proposed by Stubbe and co-workers [Harris, G., Ashley, G. W., Robins, M. J., Tolman, R. L., & Stubbe, I. (1987) Biochem. 26, 1895-1902 (1987); Stubbe, J. (1990) J. Biol. Chemical 265, 5329-5332] in which they suggest that the partitioning between reduction and inactivation occurs at the level of the 2'-deoxy-3'-keto ribonucleotide intermediate.

IT 150993-72-9P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation and ribonucleotide diphosphate reductase of Corynebacterium nephridii inhibition by, enzyme mechanism in relation to) 150993-72-9 CAPLUS

RN 150993-72-9 CAPLUS
CN Adenosine 5'-(trihydrogen diphosphate), 2'-C-methyl- (9CI) (CA INDEX NAME)

6-methylaminopurine

6-dimethylaminopurine